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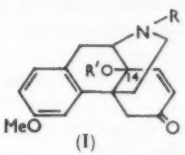
927. 14-*Hydroxynorcodeine and its Derivatives.*

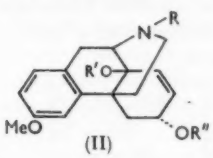
By A. C. Currie, G. T. Newbold, and F. S. Spring.

Reduction of 14-acyloxy-*N*-cyanonorcodeine derivatives by lithium aluminium hydride gives 14-hydroxynorcodeine. *N*-Acyl derivatives of the latter compound are prepared from the corresponding 14-acyloxy-*N*-cyano-compound by acyl migration. Reduction of the *N*-acyl compounds with lithium aluminium hydride gives the *N*-alkyl-14-hydroxynorcodeines.

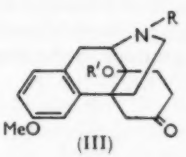
Reaction of 14-acetoxycodeinone (I; R = Me, R′ = Ac) with cyanogen bromide [1] affords 14-acetoxy-*N*-cyanonorcodeinone (I; R = CN, R′ = Ac) contrary to the claim [2] that *N*-cyano-14-hydroxynorcodeinone was so formed. Attempts to obtain the latter by the reaction between cyanogen bromide and 14-hydroxycodeinone gave a quaternary salt. However, 14-acetoxy- and 14-benzoyloxy-*N*-cyanonorcodeine 6-acetate (II; R = CN, R′ = Ac or Bz, R″ = Ac), 14-acetoxy-*N*-cyanodihydronorcodeinone (III; R = CN, R′ = Ac), *N*-cyano-14-propionyloxynorcodeinone (I; R = CN, R′ = Et·CO), and 14-*n*-butyryloxy-*N*-cyanonorcodeinone (I; R = CN, R′ = Pr·CO) were all prepared from the corresponding *N*-methyl compounds by treatment with cyanogen bromide.



(I)



(II)



(III)

14-Acetoxy-*N*-cyanonorcodeine (II; R = CN, R′ = Ac, R″ = H) was prepared from 14-acetoxy-*N*-cyanonorcodeinone by reduction with sodium borohydride. It was also formed in low yield by the action of this reagent or pyridine in methanol on 14-acetoxy-*N*-cyanonorcodeine 6-acetate.

Lithium aluminium hydride which converts the *N*-cyano-derivative of a secondary amine into the related amine,[3] when used for the reduction of 14-acetoxy-*N*-cyanonorcodeinone and 14-acetoxy-*N*-cyanonorcodeine 6-acetate yielded 14-hydroxynorcodeine (II; R = R′ = R″ = H) which was smoothly oxidised by activated manganese dioxide to 14-hydroxynorcodeinone (I; R = R′ = H), m. p. 185—187°. The compound, m. p. 218° (decomp.), obtained by hydrolysis of 14-acetoxy-*N*-cyanonorcodeinone with mineral acid and described as 14-hydroxynorcodeinone [4] was obtained in our hands as a gum and appears to be heterogeneous, its infrared spectrum showing weak bands in the *O*-acetyl region. Acetylation of the gum gives 14-acetoxy-*N*-acetylnorcodeinone (I; R = R′ = Ac), the acetylation product of 14-hydroxynorcodeinone, m. p. 185—187°. Hydrolysis of 14-acetoxy-*N*-cyanodihydronorcodeinone by mineral acid gave in poor yield 14-hydroxydihydronorcodeinone (III; R = R′ = H), m. p. 175—176°, previously described as an oil.[4] All the secondary amines described crystallise with difficulty and in very poor yield although the infrared spectra show the crude reaction products to be substantially homogeneous.

14-Acetoxy-*N*-cyanonorcodeine acetate in hot aqueous acetic acid gave a compound, m. p. 249—250°, also obtained by the action of acetic anhydride on 14-hydroxynorcodeine. This compound was unaffected by manganese dioxide and since its infrared spectrum shows bands in the hydroxyl, *O*-acetyl, and *N*-acetyl regions it must be *N*-acetyl-14-hydroxynorcodeine 6[6]-acetate (II; R′ = H, R = R″ = Ac). Both this compound and

[1] *Org. Synth.*, Coll. Vol. II, p. 150.
[2] Freund and Speyer, *J. prakt. Chem.*, 1916, **94**, 135.
[3] Prelog, McKusick, Merchant, Julia, and Wilhelm, *Helv. Chim. Acta*, 1956, **39**, 498.
[4] Speyer and Sarre, *Ber.*, 1924, **57**, 1427.

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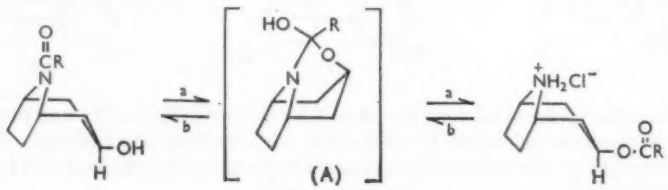
14-hydroxynorcodeine on more vigorous treatment with acetic anhydride yielded the triacetyl derivative (II; R = R′ = R″ = Ac), also obtained by refluxing 14-acetoxy-*N*-cyanonorcodeine acetate in glacial acetic acid. Attempts to hydrogenate 14-acetoxy-*N*-cyanonorcodeine acetate in acetic acid over platinum resulted in the formation of *N*-acetyl-14-hydroxynorcodeine 6-acetate which is also prepared by the action of aqueous propionic acid on the *N*-cyano-compound (II; R = CN, R′ = R″ = Ac).

Similarly 14-acetoxy-*N*-cyanonorcodeinone, when treated with aqueous propionic acid, gave *N*-acetyl-14-hydroxynorcodeinone (I; R = Ac, R′ = H), vigorous acetylation of which gave 14-acetoxy-*N*-acetylnorcodeinone. The latter was also obtained on refluxing a glacial acetic acid solution of 14-acetoxy-*N*-cyanonorcodeinone. *N*-Acetyldihydro-14-hydroxynorcodeinone (III; R = Ac, R′ = H) was prepared by the action of aqueous acetic or propionic acid on 14-acetoxy-*N*-cyanodihydronorcodeinone, and with glacial acetic acid the latter gave 14-acetoxy-*N*-acetyldihydronorcodeinone (III; R = R′ = Ac), the acetylation product of both *N*-acetyl-14-hydroxy- and 14-hydroxy-dihydronorcodeinone.

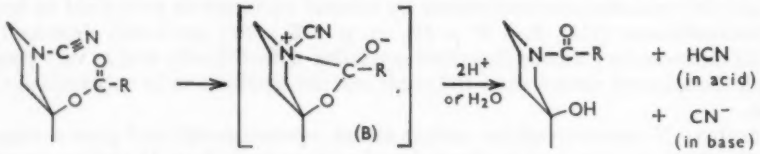
The mechanism of the formation of *N*-acetyl derivatives from 14-acetoxy-*N*-cyano-compounds must involve migration of the *O*-acetyl group. In contrast with this work, acyl groups are known to migrate from nitrogen to oxygen under acid catalysis [5] and studies of the mechanisms of the reactions have indicated that they probably proceed through cyclic intermediates.[6] Nickon and Fieser [5] postulate the intermediate (A) in the migrations in the tropine series.



a, HCl. b, K_2CO_3.

Since the formation of *N*-acetylcodeine derivatives from the 14-acetoxy-*N*-cyano-compounds can take place under anhydrous acid conditions and since, in most of these hydrolyses, mixtures of 14-acetoxy-*N*-cyano- and *N*-acetyl-14-hydroxy, but no >NH, compounds are formed it seems likely that the reaction takes place synchronously and probably through an intermediate (B), rather than by hydrolysis of the *N*-cyano-group to give, first, $>N\cdot CO_2H$ and then >NH, with subsequent acyl migration.

The reverse process of migration of the acetyl group, namely, from oxygen to nitrogen, proceeds under base catalysis [5] for the tropine alkaloids. Treatment of *N*-acetyl-14-hydroxynorcodeine acetate with base gave intractable material, the infrared spectrum



of which showed that this process may occur to some extent. However, treatment of 14-acetoxy-*N*-cyanodihydronorcodeinone (III; R = CN, R′ = Ac) with 1% potassium hydroxide in methanol gave *N*-acetyl-14-hydroxydihydronorcodeinone (III; R = Ac, R′ = H). That migration took place under basic conditions was confirmed by the action

[5] Nickon and Fieser, *J. Amer. Chem. Soc.*, 1952, **74**, 5566.
[6] Fodor and Kiss, *J. Amer. Chem. Soc.*, 1950, **72**, 3495; Welsh, *ibid.*, 1949, **71**, 3500; Philips and Baltzly, *ibid.*, 1947, **69**, 200; van Tamelen, *ibid.*, 1951, **73**, 5773.

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of 1% potassium hydroxide in methanol on 14-acetoxy-*N*-cyanonorcodeine or its acetate, which gave *N*-acetyl-14-hydroxynorcodeine (II; R = Ac, R′ = R″ = H); manganese dioxide oxidation then gave *N*-acetyl-14-hydroxynorcodeinone. With αβ-unsaturated ketones, however, the action of basic reagents gives intractable material, the infrared spectrum showing a band in the saturated ketone region.

This series of reactions demonstrates, for the first time experimentally, the close proximity of the nitrogen atom to the 14-oxygen atom in 14-hydroxycodeinone and provides a general route to *N*-acyl derivatives of 14-hydroxynorcodeine.

N-Cyano-14-propionyloxynorcodeinone, when refluxed with aqueous acetic or propionic acid, gave 14-hydroxy-*N*-propionylnorcodeinone (I; R = Et·CO, R′ = H). Reduction of the latter by sodium borohydride, followed by reaction with propionic anhydride, yielded *N*-propionyl-14-propionyloxynorcodeine 6-propionate (II; R = R′ = R″ = Et·CO) also prepared as follows: Treatment of 14-hydroxynorcodeine with, successively, propionic anhydride, sodium borohydride, and 1% methanolic potassium hydroxide gave a gum whose infrared spectrum shows bands in the *N*-acyl and hydroxyl regions; heating this gum with propionic anhydride afforded *N*-propionyl-14-propionyloxynorcodeine 6-propionate in good yield.

Similarly 14-butyryloxy-*N*-cyanonorcodeinone gave a gum (*N*-acyl and hydroxyl absorption), oxidised by active manganese dioxide to *N*-butyryl-14-hydroxynorcodeinone (I; R = Pr·CO, R′ = H), an amorphous powder, which was also obtained by refluxing an aqueous-butyric acid solution of 14-butyryloxy-*N*-cyanonorcodeinone.

Reduction of either *N*-acetyl-14-hydroxynorcodeine acetate or its 14-acetate (II; R = R″ = Ac, R′ = H or Ac) with lithium aluminium hydride afforded *N*-ethyl-14-hydroxynorcodeine (II; R = Et, R′ = R″ = H). The latter on mild acetylation yielded 14-acetoxy-*N*-ethylnorcodeine and on more vigorous acetylation gave the diacetate; both are hydrolysed by alkali to *N*-ethyl-14-hydroxynorcodeine. Oxidation of the latter acetate by manganese dioxide afforded *N*-ethyl-14-hydroxynorcodeinone (I; R = Et, R′ = H), the reverse change being effected by reduction with sodium borohydride. Similar reduction of 14-acetoxy-*N*-ethylnorcodeinone (I; R = Et, R′ = Ac) gave 14-acetoxy-*N*-ethylnorcodeine. Treatment of 14-acetoxy-*N*-ethylnorcodeine acetate with cyanogen bromide gave 14-acetoxy-*N*-cyanonorcodeine acetate.

Reduction of *N*-propionyl-14-propionyloxynorcodeine propionate by lithium aluminium hydride yielded 14-hydroxy-*N*-propylnorcodeine (II; R = Pr^n, R′ = R″ = H) which with activated manganese dioxide gave 14-hydroxy-*N*-propylnorcodeinone (I; R = Pr^n, R′ = H).

Experimental

Rotations were measured for chloroform solutions. Light petroleum, where unspecified, had b. p. 60—80°. Infrared spectra were determined for Nujol mulls, and identities were confirmed by infrared comparison.

14-*Acetoxy*-N-*cyanonorcodeine* 6-*Acetate*.—14-Acetoxycodeine acetate (6 g.) was heated with cyanogen bromide [1] (10 g.) for 3 min. at 100°. After cooling, ethanol (20 c.c.) was added and the mixture filtered. The solid product was washed with ethanol (40 c.c.) and crystallised from chloroform–methanol, to give 14-*acetoxy*-N-*cyanonorcodeine* 6-*acetate* (5 g.) as prisms, m. p. 190°, $[\alpha]_D$ −123° (*c* 0·8), $\nu_{max.}$ 2222 (C≡N), 1730 cm.$^{-1}$ (ester C=O) (Found: C, 64·6; H, 5·2; N, 6·6. $C_{22}H_{22}N_2O_6$ requires C, 64·4; H, 5·4; N, 6·8%).

14-*Acetoxy*-N-*cyanonorcodeinone*.—(*a*) 14-Acetoxycodeinone (4 g.) was heated with cyanogen bromide (8 g.) for 6 min. at 100°. Addition of ethanol gave a solid which on crystallisation from chloroform–ethanol gave 14-*acetoxy*-N-*cyanonorcodeinone* (3·5 g.) as needles, m. p. 260—262°, $[\alpha]_D$ −60° (*c* 1·9), $\nu_{max.}$ 2222 cm.$^{-1}$ (C≡N), 1739 (ester (C=O), and 1686 cm.$^{-1}$ (C:C·C=O) (Found: C, 65·9; H, 4·9. $C_{20}H_{18}N_2O_5$ requires C, 65·6; H, 4·95%).

(*b*) 14-Acetoxycodeinone (5 g.) in chloroform (400 c.c.) was refluxed for 2 hr. with cyanogen bromide (20 g.) in chloroform (200 c.c.). Evaporation gave a gum which crystallised from chloroform–methanol to give 14-acetoxy-*N*-cyanonorcodeinone (4 g.) as prismatic needles, m. p. and mixed m. p. 260—262°.

14-*Acetoxy*-N-*cyanonorcodeine*.—(*a*) To a solution of 14-acetoxy-*N*-cyanonorcodeinone (1 g.) in dioxan (75 c.c.) was added sodium borohydride (0·5 g.) in water (10 c.c.). The mixture was stirred for 2 hr., diluted with water (500 c.c.), and extracted with chloroform. The gum left on removal of the chloroform crystallised from chloroform–light petroleum, to give 14-*acetoxy*-N-*cyanonorcodeine* (0·8 g.) as prisms, m. p. 220—222°, $[\alpha]_D$ −69° (*c* 0·9), $\nu_{max.}$ 3333 (OH), 2212 (C≡N), 1730 cm.$^{-1}$ (ester C=O) (Found: C, 65·2, 65·7; H, 5·0, 5·7. $C_{20}H_{20}N_2O_5$ requires C, 65·2; H, 5·5%).

(*b*) 14-Acetoxy-*N*-cyanonorcodeine acetate (2 g.) was reduced with sodium borohydride as described above. The product on crystallisation from chloroform–methanol returned starting material (1·8 g.). From the mother-liquors, 14-acetoxy-*N*-cyanonorcodeine (0·1 g.) was obtained as prisms, m. p. and mixed m. p. 220—222°.

(*c*) 14-Acetoxy-*N*-cyanonorcodeine acetate (0·2 g.) in methanol (75 c.c.) was refluxed for 5 hr. with pyridine (4 c.c.). Removal of the solvent, followed by crystallisation from chloroform–methanol, gave 14-acetoxy-*N*-cyanonorcodeine (0·15 g.) as prisms, m. p. and mixed m. p. 220—222°.

14-Acetoxy-*N*-cyanonorcodeine gave its 6-acetate and with manganese dioxide gave 14-acetoxy-*N*-cyanonorcodeinone.

14-*Acetoxy*-N-*cyanodihydronorcodeinone*.—14-Acetoxydihydronorcodeinone (10 g.) in chloroform (500 c.c.) was refluxed with cyanogen bromide (30 g.) in chloroform (200 c.c.). Evaporation followed by addition of methanol gave 14-acetoxy-*N*-cyanodihydronorcodeinone as prisms, m. p. and mixed m. p. 260° (decomp.). The authentic specimen was kindly provided by Dr. F. R. Smith of Messrs. T. and H. Smith Ltd., Edinburgh.

Preparation of 14-*Acyloxy*-N-*cyanonorcodeine Derivatives*.—The following 14-acyloxy-*N*-cyanonorcodeine derivatives were obtained in 80—90% yields from the corresponding 14-acyloxycodeine derivatives as described for the preparation of 14-acetoxy-*N*-cyanonorcodeinone (method *b*):

N-*Cyano*-14-*propionyloxynorcodeinone* (from chloroform–light petroleum) as prisms, m. p. 220—221°, $[\alpha]_D$ −46·5° (*c* 0·8), $\nu_{max.}$ 2200 (C≡N) 1680 (C=C·C=O), 1725 cm.$^{-1}$ (ester C=O) (Found: C, 66·4; H, 5·3. $C_{21}H_{20}N_2O_5$ requires C, 66·3; H, 5·3%).

14-*Butyryloxy*-N-*cyanonorcodeinone* (from chloroform–light petroleum) as prisms, m. p. 179—180°, $[\alpha]_D$ −40° (*c* 0·8), $\nu_{max.}$ 2200 (C≡N), 1680 (C=C·C=O), 1725 cm.$^{-1}$ (ester C=O) (Found: C, 67·3; H, 5·75. $C_{22}H_{22}N_2O_5$ requires C, 67·0; H, 5·6%).

14-*Benzoyloxy*-N-*cyanonorcodeine acetate* (from chloroform–ethanol) as needles, m. p. 220°, $[\alpha]_D$ −117° (*c* 0·7), $\nu_{max.}$ 2250 (C≡N), 1715, 1740 cm.$^{-1}$ (ester C=O) (Found: C, 68·6; H, 5·0; N, 6·6. $C_{27}H_{24}N_2O_6$ requires C, 68·6; H, 5·1; N, 6·2%).

14-*Hydroxynorcodeine*.—(*a*) 14-Acetoxy-*N*-cyanonorcodeinone (478 mg.) was extracted from a Soxhlet thimble on to lithium aluminium hydride (500 mg.) in boiling ether (200 c.c.). After 66 hr. solution was complete, and the cooled solution was treated with water and chloroform to decompose the excess of lithium aluminium hydride, then filtered through kieselguhr, and the organic layer was evaporated to a gum which crystallised from chloroform–light petroleum–ethanol, giving 14-*hydroxynorcodeine* as prisms, m. p. 203°, $[\alpha]_D$ −101° (*c* 2·0), $\nu_{max.}$ 3226 cm.$^{-1}$ (OH) (Found: C, 66·6; H, 6·8. $C_{17}H_{19}NO_4,\frac{1}{2}C_2H_5{\cdot}OH$ requires C, 66·6; H, 6·8%).

Recrystallisation from chloroform–methanol gave prismatic needles of a different *solvate*, m. p. 203° (Found: C, 65·9; H, 6·8. $C_{17}H_{19}NO_4,\frac{1}{2}CH_3{\cdot}OH$ requires C, 66·2; H, 6·7%).

(*b*) 14-Acetoxy-*N*-cyanonorcodeine acetate (4·5 g.) in suspension in anhydrous ether (1 l.) was cooled to room temperature and a suspension of lithium aluminium hydride (4 g.) in anhydrous ether (200 c.c.) added in portions. The mixture was then refluxed for 2 hr., cooled, and worked up as described in preparation (*a*). The gum left on removal of the solvent crystallised from chloroform–methanol to give 14-hydroxynorcodeine (1 g.) as needles, m. p. and mixed m. p. 203°.

14-*Hydroxynorcodeinone*.—14-Hydroxynorcodeine (200 mg.) in chloroform (10 c.c.) was stirred for 1 hr. with active manganese dioxide (1 g.). The filtered solution was evaporated and the gum obtained crystallised from chloroform–methanol to give 14-*hydroxynorcodeinone* (150 mg.), m. p. 185—187°, $[\alpha]_D$ −40° (*c* 0·2), $\nu_{max.}$ 3390 (OH), 1678 cm.$^{-1}$ (C:C·C=O) (Found: C, 68·7; H, 5·5. $C_{17}H_{17}NO_4$ requires C, 68·2; H, 5·7%).

Dihydro-14-*hydroxynorcodeinone*.—14-Acetoxy-*N*-cyanodihydronorcodeinone (5 g.) in 25% sulphuric acid (50 c.c.) was refluxed for 4 hr. The cooled solution was diluted with water (500 c.c.) and, after addition of ammonia (*d* 0·88), the base was isolated in chloroform. Removal

of the solvent under a vacuum at room temperature, followed by addition of methanol and concentration of the solution to low bulk under a vacuum, gave dihydro-14-hydroxynorcodeinone (1 g.) as needles, m. p. 174—175°, $[\alpha]_D$ −205° (*c* 0·4), $\nu_{max.}$ 3280 (OH), 1713 cm.$^{-1}$ (C=O). A satisfactory analysis could not be obtained for this compound.

Dihydro-14-hydroxynorcodeinone hydriodide (250 mg.), prepared as described by Speyer and Sarre,[4] was dissolved in water (200 c.c.), ammonia (*d* 0·88) added, and the base extracted with chloroform. The gum obtained crystallised from chloroform–methanol to give dihydro-14-hydroxynorcodeinone (35 mg.) as needles, m. p. and mixed m. p. 174—175°.

N-Acetyl-14-hydroxynorcodeine 6-Acetate.—(*a*) 14-Hydroxynorcodeine (100 mg.) was heated on the steam bath for 1 hr. with acetic anhydride (5 c.c.). The mixture was cooled, taken up in chloroform, and shaken with water and ammonia (*d* 0·88). The chloroform solution was washed with water and evaporated. The gum obtained crystallised from chloroform–methanol to give *N-acetyl-14-hydroxynorcodeine 6-acetate* (80 mg.) as needles, m. p. 249—250° (decomp.), $[\alpha]_D$ −206° (*c* 0·5), $\nu_{max.}$ 3311 (OH), 1713 (ester C=O), 1613 cm.$^{-1}$ (*N*-acetyl C=O) (Found: C, 65·35; H, 6·4. $C_{21}H_{23}O_6N$ requires C, 65·4; H, 6·0%).

(*b*) 14-Acetoxy-*N*-cyanonorcodeine acetate (5 g.) in acetic acid (245 c.c.) and water (105 c.c.) was refluxed for 4 hr. The cooled solution was basified and the solid extracted with chloroform, to yield on evaporation a gum which crystallised from chloroform–methanol; this gave *N*-acetyl-14-hydroxynorcodeine acetate (2·5 g.) as needles, m. p. and mixed m. p. 249—250° (decomp.). A further crop (2·0 g.) was obtained by recycling the mother liquor with aqueous acetic acid.

(*c*) 14-Acetoxy-*N*-cyanonorcodeine acetate (350 mg.) in (i) glacial acetic acid (75 c.c.) and (ii) 50% aqueous acetic acid (75 c.c.) was shaken with hydrogen and platinum oxide (150 mg.). In each case starting material (90%) was returned but the mother liquors yielded from chloroform–light petroleum *N*-acetyl-14-hydroxynorcodeine acetate (10%) as needles, m. p. and mixed m. p. 249—250° (decomp.).

(*d*) 14-Acetoxy-*N*-cyanonorcodeine acetate (750 mg.) in propionic acid (35 c.c.) and water (15 c.c.) was refluxed for 14 hr. After working up in the usual way, the gum obtained crystallised from chloroform–methanol to give *N*-acetyl-14-hydroxynorcodeine acetate as needles, m. p. and mixed m. p. 249—250° (decomp.).

14-Acetoxy-N-acetylnorcodeine 6-Acetate.—(*a*) *N*-Acetyl-14-hydroxynorcodeine acetate (300 mg.) in acetic anhydride (15 c.c.) was refluxed for 2 hr. The cooled solution was worked up through chloroform in the usual way and the gum obtained crystallised from chloroform–methanol to give *14-acetoxy-N-acetylnorcodeine acetate* (300 mg.) as needles, m. p. 185—186°, $[\alpha]_D$ −167° (*c* 0·4), $\nu_{max.}$ 1727 (ester C=O), 1634 cm.$^{-1}$ (*N*-acetyl C=O) (Found: C, 63·8; H, 6·2. $C_{23}H_{25}NO_{7,\frac{1}{4}}CH_3{\cdot}OH$ requires C, 63·6; H, 6·1%).

(*b*) 14-Hydroxynorcodeine (35 mg.) in acetic anhydride (5 c.c.) was refluxed for 2 hr. The gum obtained after working up through chloroform crystallised from chloroform–methanol, to give 14-acetoxy-N-acetylnorcodeine acetate, m. p. and mixed m. p. 185—186°.

(*c*) 14-Acetoxy-*N*-cyanonorcodeine acetate (250 mg.) in acetic acid (35 c.c.) and acetic anhydride (1 c.c.) was refluxed for 5 hr. After removal of the solvent under a vacuum the residue crystallised from chloroform–methanol to give 14-acetoxy-*N*-acetylnorcodeine acetate (200 mg.) as needles, m. p. and mixed m. p. 185—186°.

14-Acetoxy-N-acetylnorcodeinone.—(*a*) 14-Hydroxynorcodeinone (80 mg.) in acetic anhydride (10 c.c.) was refluxed for 2 hr. After cooling and basifying, the solid was extracted with chloroform to give a gum which crystallised from chloroform–light petroleum–ethanol to give *14-acetoxy-N-acetylnorcodeinone* (80 mg.) as needles, m. p. 174—176°, $[\alpha]_D$ −104° (*c* 0·6), $\nu_{max.}$ 1737 (ester C=O), 1681 (C:C·C=O), 1639 cm.$^{-1}$ (*N*-acetyl C=O) (Found: C, 65·4; H, 5·5. $C_{21}H_{21}NO_6$ requires C, 65·8; H, 5·5%).

(*b*) 14-Acetoxy-*N*-cyanonorcodeinone (1 g.) in acetic acid (70 c.c.) and water (30 c.c.) was refluxed for 4 hr. The product obtained by basification and extraction with chloroform was refluxed with acetic anhydride (20 c.c.) for 2 hr. The cooled solution was made basic with ammonia (*d* 0·88) and worked up through chloroform–light petroleum–ethanol to give 14-acetoxy-*N*-acetylnorcodeinone (0·8 g.) as needles, m. p. and mixed m. p. 174—176°.

(*c*) 14-Acetoxy-*N*-cyanonorcodeinone (300 mg.) in acetic acid (35 c.c.) and acetic anhydride (0·5 c.c.) was refluxed for 5 hr. After removal of the solvent, the gum crystallised from ether–ethanol to give 14-acetoxy-*N*-acetylnorcodeinone (250 mg.) as needles, m. p. and mixed m. p. 176°.

(*d*) 14-Acetoxy-*N*-cyanonorcodeinone (12 g.) in 25% sulphuric acid (15 c.c.) was refluxed for 3 hr. After boiling with charcoal, the solution was filtered, made basic, and extracted with chloroform. The gum obtained was refluxed with acetic anhydride (20 c.c.) for 2 hr., then cooled and worked up through chloroform. The gum obtained crystallised from chloroform–light petroleum–ethanol to give 14-acetoxy-*N*-acetylnorcodeinone as needles, m. p. and mixed m. p. 174—176°.

N-*Acetyl*-14-*hydroxynorcodeinone*.—14-Acetoxy-*N*-cyanonorcodeinone (5 g.) in propionic acid (140 c.c.) and water (60 c.c.) was refluxed for 20 hr. The cooled solution was made basic with ammonia (*d* 0·88) and then extracted with chloroform. After removal of the solvent the gum crystallised from chloroform–methanol to give N-*acetyl*-14-*hydroxynorcodeinone* (1·5 g.) as prisms, m. p. 222—223°, $[\alpha]_D$ −221° (*c* 0·25), $\nu_{max.}$ 3333 (OH), 1695 (C:C·C=O), 1600 cm.$^{-1}$ (*N*-acetyl C=O) (Found: C, 66·8; H, 5·6. $C_{19}H_{19}NO_5$ requires C, 66·85; H, 5·6%). This gives the 14-acetoxy-compound, m. p. and mixed m. p. 174—176°.

14-*Acetoxy*-N-*acetylnorcodeine*.—14-Acetoxy-*N*-acetylnorcodeinone (200 mg.) in dioxan (10 c.c.) was stirred for 2 hr. with a solution of sodium borohydride (200 mg.) in water (2 c.c.). The solution was worked up in the usual way through chloroform to give a gum which crystallised from chloroform–light petroleum to give 14-*acetoxy*-N-*acetylnorcodeine* (150 mg.) as prisms, m. p. 195°, $[\alpha]_D$ −73° (*c* 0·15), $\nu_{max.}$ 1730 (ester C=O), 1630 cm.$^{-1}$ (*N*-acetyl C=O) (Found: C, 66·0; H, 6·0. $C_{21}H_{23}NO_6$ requires C, 65·45; H, 6·0%).

N-*Acetyl*-14-*hydroxynorcodeine*.—(*a*) 14-Acetoxy-*N*-cyanonorcodeine acetate (1 g.) was refluxed for 6 hr. with potassium hydroxide (1 g.) in methanol (99 c.c.) and water (1 c.c.). After addition of water (600 c.c.), the solution was extracted with chloroform (4 × 50 c.c.). The chloroform solution was washed with water (2 × 100 c.c.), dried (Na_2SO_4), and evaporated under a vacuum. The solid obtained was triturated with anhydrous ether to give amorphous N-*acetyl*-14-*hydroxynorcodeine* (700 mg.), m. p. 115—120°, $[\alpha]_D$ −113·5° (*c* 0·3), $\nu_{max.}$ 3333 (OH), 1618 cm.$^{-1}$ (*N*-acetyl C=O) (Found: C, 62·3; H, 6·7. $C_{19}H_{21}NO_5,H_2O$ requires C, 63·1; H, 6·4%). 14-Acetoxy-*N*-cyanonorcodeine (0·5 g.), similarly treated, gave the same product.

(*b*) *N*-Acetyl-14-hydroxynorcodeinone (135 mg.) in dioxan (10 c.c.) was stirred for 2 hr. with sodium borohydride (100 mg.) in water (3 c.c.). After addition of water (500 c.c.) the solution was extracted with chloroform to give, on removal of the solvent, a gum which was triturated with anhydrous ether to give amorphous *N*-acetyl-14-hydroxynorcodeine, m. p. and mixed m. p. 115—120°.

N-*Acetyl*-14-*hydroxynorcodeinone*.—*N*-Acetyl-14-hydroxynorcodeine (200 mg.) in chloroform (10 c.c.) was stirred at room temperature for 1 hr. with active manganese dioxide (1 g.). The filtered solution was evaporated and the residue crystallised from chloroform–methanol to give *N*-acetyl-14-hydroxynorcodeinone (100 mg.) as prisms, m. p. and mixed m. p. 222—223°.

N-*Acetyldihydro*-14-*hydroxynorcodeinone*.—(*a*) 14-Acetoxy-*N*-cyanodihydronorcodeinone (4 g.) in 70% acetic acid (300 c.c.) was refluxed for 4 hr. The solution was cooled and made basic with ammonia (*d* 0·88) and shaken with chloroform (100 c.c.). The chloroform layer was washed with water, dried (Na_2SO_4), and evaporated in a vacuum to a gum which crystallised from chloroform–methanol, giving N-*acetyldihydro*-14-*hydroxynorcodeinone* (3 g.) as prisms, m. p. 254—255°, $[\alpha]_D$ −260° (*c* 1·2), $\nu_{max.}$ 3225 (OH), 1725 (C=O), 1612 cm.$^{-1}$ (*N*-acetyl C=O) (Found: C, 64·7; H, 6·1. $C_{19}H_{21}NO_5,\frac{1}{2}H_2O$ requires C, 64·8; H, 6·3%). Use of 70% propionic acid gave the same product.

(*c*) 14-Acetoxy-*N*-cyanodihydronorcodeinone (750 mg.) was refluxed for 4 hr. with a solution of potassium hydroxide (0·7 g.) in methanol (70 c.c.) and water (1 c.c.). The cooled solution was diluted with water (700 c.c.), and the base, extracted with chloroform, crystallised from chloroform–light petroleum, to give 14-acetoxy-*N*-acetyldihydronorcodeinone (150 mg.) as prisms, m. p. and mixed m. p. 254—258°.

Dihydro-N-*propionyl*-14-*propionyloxynorcodeinone*.—Dihydro-14-hydroxynorcodeinone (200 mg.) in propionic anhydride (10 c.c.) was heated on the steam bath for 3 hr. The cooled solution was taken up in chloroform, washed with ammonia (*d* 0·88) and water, dried (Na_2SO_4), and evaporated. The resulting gum crystallised from chloroform–light petroleum to give the *dipropionyl-ketone* (150 mg.) as prisms, m. p. 180—181°, $[\alpha]_D$ −296° (*c* 1·0), $\nu_{max.}$ 1725 (ester C=O), 1640 cm.$^{-1}$ (*N*-propionyl C=O) (Found: C, 66·75; H, 6·9. $C_{23}H_{27}NO_6$ requires C, 66·8; H, 6·6%).

14-*Hydroxy*-N-*propionylnorcodeinone*.—(*a*) *N*-Cyano-14-propionyloxynorcodeinone (5 g.) in

70% propionic acid (100 c.c.) was refluxed for 20 hr. The solution was worked up in the usual way to give a gum which, from chloroform–methanol, gave 14-*hydroxy*-N-*propionylnorcodeinone* (1·5 g.) as prisms, m. p. 229—230°, $[\alpha]_D$ −172·5° (*c* 0·6), $\nu_{max.}$ 3195 (OH), 1666 (C:C·C=O), 1612 cm.$^{-1}$ (*N*-propionyl C=O) (Found: C, 67·9; H, 5·6. $C_{20}H_{21}NO_5$ requires C, 67·6; H, 6·0%). Use of 70% acetic acid gave the same product.

N-*Propionyl*-14-*propionyloxynorcodeine* 6-*Propionate*.—(*a*) 14-Hydroxynorcodeine (5 g.) was heated on the steam bath for 3 hr. with propionic anhydride (20 c.c.). The cooled solution was made basic with ammonia (*d* 0·88) and extracted with chloroform. The gum obtained on removal of the solvent was filtered in benzene through alumina. After elution with benzene (500 c.c.), and removal of the solvent, the gum obtained crystallised from chloroform–light petroleum to give the *tripropionyl derivative* (1·5 g.), prisms, m. p. 157—158°, $[\alpha]_D$ −145° (*c* 2·0), $\nu_{max.}$ 1724 (ester C=O), 1640 cm.$^{-1}$ (*N*-propionyl C=O) (Found: C, 66·35; H, 6·7. $C_{26}H_{31}NO_7$ requires C, 66·5; H, 6·7%).

(*b*) 14-Hydroxy-*N*-propionylnorcodeinone (200 mg.) in dioxan (20 c.c.) was stirred with sodium borohydride (200 mg.) in water (5 c.c.) for 2 hr. After working up in the usual way, the gum obtained was heated for 3 hr. on the steam bath with propionic anhydride (5 c.c.). Removal of the anhydride under a vacuum gave a gum which crystallised from chloroform–light petroleum to give the preceding product.

(*c*) *N*-Cyano-14-propionyloxynorcodeinone (400 mg.) was similarly reduced to a gum that was refluxed for 12 hr. with potassium hydroxide (250 mg.) in methanol (25 c.c.) and water (0·5 c.c.). The solid product (230 mg.), $\nu_{max.}$ 3333 (OH), 1612 cm.$^{-1}$ (*N*-propionyl), was heated on the steam bath for 3 hr. with propionic anhydride (5 c.c.), and the resulting gum crystallised from chloroform–light petroleum to give the tripropionyl derivative (130 mg.), prisms, m. p. and mixed m. p. 157—158°.

N-*Butyryl*-14-*hydroxynorcodeinone*.—(*a*) 14-Butyryloxy-*N*-cyanonorcodeinone (0·6 g.) in butyric acid (35 c.c.) and water (15 c.c.) was refluxed for 18 hr. The cooled solution was made basic with ammonia (*d* 0·88), and the gum obtained on extraction with chloroform was triturated with anhydrous ether to give amorphous *N*-butyryl-14-hydroxynorcodeinone (0·6 g.), m. p. 185—190°, $[\alpha]_D$ −162° (*c* 0·2), $\nu_{max.}$ 3333 (OH), 1685 (C:C·C=O), 1613 cm.$^{-1}$ (*N*-acyl C=O). A satisfactory analysis was not obtained.

(*b*) 14-Butyryloxy-*N*-cyanonorcodeinone (3 g.) in dioxan (100 c.c.) was stirred for 2 hr. with sodium borohydride (1·5 g.) in water (20 c.c.). After being worked up through chloroform the gum obtained was refluxed for 18 hr. with potassium hydroxide (1 g.) in methanol (100 c.c.) and water (1 c.c.). The cooled solution was diluted with water (750 c.c.) and extracted with chloroform (6 × 50 c.c.). The bulked chloroform layers yielded a gum (1·8 g.), $\nu_{max.}$ 3333 (OH), 1613 cm.$^{-1}$ (*N*-butyryl), which was stirred in chloroform (20 c.c.) for 1 hr. with active manganese dioxide (4·5 g.). The filtered solution was evaporated and the residue on trituration with anhydrous ether gave amorphous *N*-butyryl-14-hydroxynorcodeinone (1·5 g.), m. p. and mixed m. p. 185—190°.

N-*Ethyl*-14-*hydroxynorcodeine*.—(*a*) *N*-Acetyl-14-hydroxynorcodeine acetate (100 mg.) in suspension in anhydrous ether (200 c.c.) was cooled and lithium aluminium hydride (250 mg.) in anhydrous ether (20 c.c.) added. The mixture was refluxed for 2 hr., then cooled, and the excess of hydride destroyed by chloroform and ice. The filtered solution was shaken with water and the chloroform–ether layer separated. After removal of the solvent, the gum crystallised from chloroform–light petroleum to give N-*ethyl*-14-*hydroxynorcodeine* (90 mg.), prisms, m. p. 128°, $[\alpha]_D$ −105° (*c* 0·3), $\nu_{max.}$ 3448, 3226 cm.$^{-1}$ (OH) (Found: C, 69·75; H, 7·3. $C_{19}H_{23}NO_4$ requires C, 69·3; H, 7·0%). 14-Acetoxy-*N*-acetylnorcodeine and its acetate, when treated with lithium aluminium hydride as above, yielded the same alcohol, m. p. and mixed m. p. 128°.

N-*Ethyl*-14-*hydroxynorcodeinone*.—*N*-Ethyl-14-hydroxynorcodeine (60 mg.) in chloroform (5 c.c.) was stirred for 1 hr. with activated manganese dioxide. The filtered solution was evaporated to dryness and the gum crystallised from chloroform–light petroleum–ethanol to give N-*ethyl*-14-*hydroxynorcodeinone* (50 mg.), prisms, m. p. 230° (decomp.), $[\alpha]_D$ −220° (*c* 1·0), $\nu_{max.}$ 3257 (OH), 1669 cm.$^{-1}$ (C:C·C=O) (Found: C, 68·7; H, 6·7. $C_{19}H_{21}NO_4,\frac{1}{2}C_2H_5OH$ requires C, 68·55; H, 6·9%).

N-*Ethyl*-14-*hydroxynorcodeine*.—*N*-Ethyl-14-hydroxynorcodeinone (100 mg.) in dioxan (25 c.c.) was treated with a suspension of sodium borohydride (100 mg.) in water (3 c.c.) with stirring. After 2 hr., water (500 c.c.) was added, and the solid extracted with chloroform. The gum left

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on removal of the solvent crystallised from chloroform–light petroleum to give *N*-ethyl-14-hydroxynorcodeine (100 mg.), prisms, m. p. and mixed m. p. 128°.

With acetic anhydride this gave its *acetate*, prisms (from chloroform–light petroleum–ethanol), m. p. 183—185°, $[\alpha]_D$ −115° (*c* 0·2), $\nu_{max.}$ 1730 (ester C=O), 1684 cm.$^{-1}$ (C:C·C=O) (Found: C, 68·0; H, 6·3. $C_{21}H_{23}NO_5$ requires C, 68·3; H, 6·3%).

14-*Acetoxy*-N-*ethylnorcodeine*.—*N*-Ethyl-14-hydroxynorcodeine with acetic anhydride at 100° for 1 hr. gave its 14-*acetate*, needles (from chloroform–methanol), m. p. 224—225°, $[\alpha]_D$ −83° (*c* 0·3), $\nu_{max.}$ 3571 (OH), 1733 cm.$^{-1}$ (ester C=O) (Found: C, 67·7; H, 6·8. $C_{21}H_{25}NO_5$ requires C, 67·9; H, 6·8%).

14-Acetoxy-*N*-ethylnorcodeinone (350 mg.) in dioxan (20 c.c.) was reduced by sodium borohydride (200 mg.) in water (5 c.c.) to the same product.

14-*Acetoxy*-N-*ethylnorcodeine* 6-*Acetate*.—*N*-Ethyl-14-hydroxynorcodeine (100 mg.) in acetic anhydride (10 c.c.) was refluxed for 1 hr. The product was the *diacetate*, prisms (80 mg.) (from chloroform–light petroleum–ethanol), m. p. 170—171°, $[\alpha]_D$ −143° (*c* 0·4), $\nu_{max.}$ 1742, 1724 cm.$^{-1}$ (ester C=O) (Found: C, 67·15; H, 6·9. $C_{23}H_{27}NO_6$ requires C, 66·8; H, 6·6%).

14-*Acetoxy*-N-*cyanonorcodeine* 6-*Acetate*.—14-Acetoxy-*N*-ethylnorcodeine 6-acetate (100 mg.) was heated with cyanogen bromide (1 g.) for 3 min. at 100°. Crystals separated on cooling and were filtered off, washed with ethanol, and recrystallised from chloroform–methanol, giving 14-acetoxy-*N*-cyanonorcodeine acetate as prisms, m. p. and mixed m. p. 190°.

14-*Hydroxy*-N-*propylnorcodeine*.—*N*-Propionyl-14-propionyloxynorcodeine 6-propionate (400 mg.) in dry tetrahydrofuran (10 c.c.) and anhydrous ether (90 c.c.) was refluxed for 4 hr. after the addition of lithium aluminium hydride (300 mg.). The excess of hydride was destroyed by chloroform (100 c.c.) and ice, and the mixture filtered through kieselguhr. The chloroform–ether layer was separated. The product, isolated in the usual way, crystallised from chloroform–light petroleum to give 14-*hydroxy*-N-*propylnorcodeine* (300 mg.) as prisms, m. p. 111—112°, $[\alpha]_D$ −121° (*c* 1·5), $\nu_{max.}$ 3390 cm.$^{-1}$ (OH) (Found: C, 69·9; H, 7·6. $C_{20}H_{25}NO_4$ requires C, 69·95; H, 7·3%).

14-*Hydroxy*-N-*propylnorcodeinone*.—14-Hydroxy-*N*-propylnorcodeine (100 mg.) in chloroform (5 c.c.) was stirred for 1 hr. with active manganese dioxide (500 mg.). The filtered solution was evaporated and the residue crystallised from chloroform–light petroleum to give 14-*hydroxy*-N-*propylnorcodeinone* (100 mg.) as needles, m. p. 126—127°, $[\alpha]_D$ −208° (c 0·6), $\nu_{max.}$ 3333 (OH) and 1680 cm.$^{-1}$ (C:C·C=O) (Found: C, 70·4; H, 7·0. $C_{20}H_{23}NO_4$ requires C, 70·4; H, 6·8%). Its 14-*acetate* formed needles (chloroform–light petroleum–ethanol), m. p. 178°, $[\alpha]_D$ −102° (*c* 1·1), $\nu_{max.}$ 1686) C:C·C=O) and 1730 cm.$^{-1}$ (ester C=O) (Found: C, 68·8; H, 6·8. $C_{22}H_{25}NO_5$ requires C, 68·9; H, 6·6%).

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928. *The Dipole Moments of Some Acetylamino-compounds and the Preferred Conformation of the Acetylamino-Group.*

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The dipole moments of acetanilide and various nuclear-substituted acetanilides have been determined for benzene solutions at 25°. The results are interpreted as indicating that the preferred conformation is that in which the angle between the C_{ar}–N–C_{carb} and N–C_{carb}–O planes is about 30°, the oxygen atom being on the same side of the former plane as is the lone pair of electrons on the nitrogen atom.

THE dipole moments of the acetyl derivatives of arylamines are of interest in view of the possibility that even in the free molecule the carbonyl group may assume a preferred conformation relative to the C_{ar}–N–$C_{carb.}$ plane. Measurements have therefore been made of the moments of a number of these compounds in benzene solution at 25°, and the results are shown in Table 1, which also includes the corresponding values for the parent amines. The moment of acetanilide now reported is rather lower than the value

(4·01 D) deduced by Le Fèvre and Le Fèvre [1] from measurements on more concentrated solutions in benzene.

TABLE 1.

Dipole moments in benzene solution.

	μ (D)		μ (D)		μ (D)
Acetanilide	3·65	Acetylaminodurene	3·8$_4$	*p*-Toluidine	1·32 [e]
p-Chloroacetanilide	4·32	Acetyl-α-naphthylamine	3·67	*m*-Toluidine	1·45 [d]
p-Bromoacetanilide	4·36	Acetyl-β-naphthylamine	3·68	*o*-Toluidine	1·59 [d]
Acetyl-*p*-toluidine	3·74	Aniline	1·53 [a]	Aminodurene	1·45 [e]
Acetyl-*m*-toluidine	3·69	*p*-Chloroaniline	3·01 [b]	α-Naphthylamine	1·50 [f]
Acetyl-*o*-toluidine	3·71	*p*-Bromoaniline	3·01 [c]	β-Naphthylamine	1·77 [g]

[a] Few and Smith, *J.*, 1949, 753. [b] *Idem*, *J.*, 1949, 2781. [c] Smith and Walshaw, *J.*, 1957, 3217. [d] Tiganik, *Z. phys. Chem.*, 1951, **14**, *B*, 135 (recalculated). [e] Smith, *J.*, 1953, 109. [f] Smith, *J.*, 1961, 81. [g] Vasiliev and Syrkin, *Acta Physicochem. U.R.S.S.*, 1941, **14**, 414.

In some hydrogen-bonded structures the amide group is probably planar, but it seems unlikely that this is the case for the free acetanilide molecule, which shows some basic properties although it is a weaker base than water. In benzene solution the dipole moment of aniline is 1·53 D. Its dipole is effectively directed along an axis at about 48·5° to the N–C_{ar} bond and in a plane including this bond and bisecting the angle between the two N–H bonds. This moment can be resolved into components μ_a (=1·42 D) along the axis of the N–C_{ar} bond and μ_b (=1·22 D) along the axis of the lone-pair orbital.[2] The dipole moment of acetone (μ_c) is 2·78 D[3] and is directed along the C_{carb}–O bond. As a first approximation, therefore, it may be assumed that the dipole moment of acetanilide comprises the vector sum of μ_a, μ_b, and μ_c, together with an additional component μ_d acting along the C_{carb}–N bond. The latter arises through the replacement of the C–C, three C–H, and the H–N bond by the C_{carb}–N bond. If it is further assumed that the C_{ar}–N–C_{carb} angle is tetrahedral and the N–C_{carb}–O angle is 120°, the general expression for the resultant moment is

$$\mu^2 = \mu_a^2 + \mu_b^2 + \mu_c^2 + \mu_d^2 - \tfrac{1}{3}(2\mu_a\mu_b + \mu_a\mu_c + \mu_b\mu_c - 2\mu_b\mu_d + 3\mu_c\mu_d) + (1{\cdot}633\mu_a\mu_c - 0{\cdot}8165\mu_b\mu_c)\cos\phi + 1{\cdot}4142\mu_b\mu_c\sin\phi, \quad (1)$$

where ϕ is the angle between the C_{ar}–N–C_{carb} and N–C_{carb}–O planes. On substituting the values of μ_a, μ_b, and μ_c given above this reduces to

$$\cdot\mu^2 = 7{\cdot}632 + 4{\cdot}796\sin\phi + 3{\cdot}677\cos\phi + \mu_d^2 - 1{\cdot}02\mu_d. \quad (2)$$

Evidently when $\mu_d = 1{\cdot}02$ D the terms involving it cancel out, whilst for any positive value below about 1·4 D its effect on the result is small. Further, it appears very improbable that this component will have a large negative value such as to affect the resultant moment appreciably. Hence, by neglecting the terms in μ_d it is possible to calculate the resultant moment for various conformations of the acetyl group. The maximum and minimum values of μ (3·70 and 1·26 D, respectively) occur when ϕ is 52·5° and 232·5°, respectively, whilst for free rotation about the C_{carb}–N bond the calculated moment is 2·76 D.

If the hydrogen atom, the phenyl group, and the lone pair on the nitrogen atom exerted equal repulsive effects towards the approach of the methyl group or the oxygen atom of the acetyl group there would be six equivalent positions of minimum potential energy with $\phi = 30°$, 90°, 150°, 210°, 270°, and 330°, respectively, *i.e.*, I—VI. The fact that these repulsive effects will not be equal, however, must cause the potential energy wells to be of unequal depths and to be displaced slightly from this symmetrical arrangement. Further, the conformations (I) and (IV) should be favoured by the circumstance that

[1] Le Fèvre and Le Fèvre, *J.*, 1936, 1136.
[2] Smith, *J.*, 1961, 81.
[3] Wesson, "Tables of Electric Dipole Moments," Technology Press, Cambridge, Mass., 1948.

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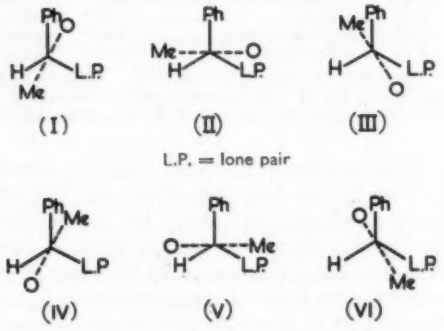
they yield the greatest overlap of the lone-pair orbital with the p_π-orbital of the C_{carb} atom, thus leading to a conjugation of this π-electron system with that of the aromatic ring. Apart from such considerations, however, the repulsion between the lone pair and the oxygen atom might cause conformation (II) to have a slightly higher potential energy than (I), whilst repulsions between the phenyl and the methyl group will raise the potential energy of (IV): form (III), where both these effects come into play may have a still higher



potential energy. Conformations (V) and (VI) would seem to be favoured sterically, but do not permit very large overlap of the lone-pair orbital with the p_π-orbital of the C_{carb} atom

From these considerations it is to be inferred that (I) should be the most favoured conformation. In this connexion it seems pertinent that Brown and Corbridge [4] found that in the crystal ϕ is 37° 54′.

The values of the dipole moment of acetanilide in the various conformations, calculated according to eqn. 2 with $\mu_d = 0$, are shown under *a* in the third column of Table 2. The

TABLE 2.

Calculated dipole moments of acetanilide and its *para*-derivatives in various conformations.

Conformation	ϕ	Calculated dipole moment (D) Acetanilide		*p*-Chloro- and *p*-bromo-acetanilide		Acetyl-*p*-toluidine	
		a	*b*	*a*	*b*	*a*	*b*
cis	0°	3·36	2·84	4·93	4·33	3·06	2·77
I	30°	3·63	3·16	5·02	4·45	3·39	3·11
	38°	3·67	3·22	4·99	4·43	3·45	3·18
II	90°	3·52	3·29	4·18	3·80	3·48	3·34
III	150°	2·62	2·59	2·23	2·21	2·83	2·89
trans	180°	1·99	2·26	1·00	1·27	2·31	2·47
IV	210°	1·43	1·56	0·44	1·07	1·79	2·01
V	270°	1·69	1·52	2·80	2·43	1·60	1·60
VI	330°	2·90	2·39	4·51	3·94	2·59	2·32

[a] Values calculated by using " idealised " valency angles. [b] Values calculated by using valency angles found in the crystal.

observed moment (3·65 D) is very near to the calculated moment for form (I) and is much greater than that for any of the other conformations. Hence it may be inferred that a conformation near to (I) predominates for the molecules in solution as well as in the crystal.

[4] Brown and Corbridge, *Acta Cryst.*, 1954, **7**, 711.

This inference receives general support from a comparison of the measured moments of derivatives of acetanilide with their calculated values, deduced by inserting the appropriate values of μ_a in eqn. 1. For *p*-chloro- and *p*-bromo-acetanilide $\mu_a = 3{\cdot}18$ D, and the calculated moment shows a much greater variation with ϕ than does that of acetanilide itself. The high observed moments for these compounds suggest that conformation (I) or (VI) must predominate and that relatively few molecules can exist in conformations (II—V) (Table 2, column 5). For acetyl-*p*-toluidine $\mu_a = 1{\cdot}05$ D, and the observed moment is higher than the calculated value for any of the conformations. Of the latter, (II) and (I) have the highest calculated moments. This result may therefore be interpreted as confirming the relative absence of the conformations (III—VI).

The moments of the same compounds have also been calculated for each conformation on the assumption that the valency angles in the molecules in solution are the same as were found by Brown and Corbridge in the acetanilide crystal, *viz.*, C_{ar}–N–$C_{carb} = 129°\ 18'$ and N–C_{carb}–O $= 121°\ 42'$. Except for *p*-chloro- and *p*-bromo-acetanilide the highest moments calculated on this basis are those for conformation (II) (cf. Table 2, values under *b*), but they are appreciably less than the measured moments. The calculated moments for (IV) are higher than those based on idealised angles, but nevertheless the values are so low that this conformation cannot make a major contribution to the structure. It is of interest, however, that with these distorted angles the moment of acetyl-*p*-toluidine in certain conformations can exceed that of acetanilide, in accordance with observation.

In the free molecules the valency angles are most probably greater than the idealised values but smaller than those observed in the crystal. The calculations are not very sensitive to the assumptions made regarding the axis of the lone-pair orbital. However, in the limiting case, probably never attained in these compounds, where the bonds around the nitrogen atom become coplanar, conformations (I) and (VI) are mirror images of one another, as are (II) and (V), and (III) and (IV). Assuming the other angles to be the same as in the crystal gives the calculated moments for acetanilide in such conformations as 3·01, 2·45, and 1·62 D, respectively. The evidence suggests, therefore, that in solution the preferred conformation is one in which ϕ is near to 30° and probably very near to the angle of 38° found in the crystal. The proportion of molecules in other conformations must be relatively small, but the nature of the assumptions made in the calculations would render any calculation of the proportions present unjustified.

The dipole moments of the other acetyl derivatives of amines studied indicate that the same general behaviour is followed as for acetanilide. Thus no essential change in the stable conformation is brought about by the presence of the second ring in acetyl-α-naphthylamine or by the *o*-methyl groups in acetyl-*o*-toluidine or acetylaminodurene.

Experimental.—The acetylamino-compounds were prepared by acetylation of the respective amines and recrystallised repeatedly from aqueous alcohol. Thiophen-free benzene was purified by repeated crystallisation, followed by drying over sodium.

The dielectric constants, refractive indices, and specific volumes of the solutions were measured at 25°. The results are shown in Table 3, where the symbols have their usual significance. For some of the compounds, and especially for acetanilide, the apparent molecular polarisation increases rapidly with increasing concentration. Molecular association is presumably responsible for this behaviour, but the number of solutions studied permits fairly accurate extrapolation of the data to zero concentration, where association effects should be absent. Hence the moments derived can be regarded as applying to the monomeric forms.

Owing to the very low solubilities of some of the compounds studied the refractive indices of the solutions differed very little from that of the solvent. Nevertheless, the $[R_D]$ values derived from these results are in good agreement with those calculated from the molecular refraction of acetanilide itself and the appropriate bond refractions of the substituents.[5] Some of the solutions of the *p*-halogenoacetanilides and of acetylaminodurene were actually supersaturated at 25°.

[5] Vogel, Cresswell, Jeffrey, and Leicester, *J.*, 1952, 514.

TABLE 3.

Polarisation data.

10^4w	ε	v	n_D
	Acetanilide		
0	2·2741	1·14460	1·4980
895	2·2841	1·14436	1·4980
1635	2·2925	1·14417	1·4981
1864	2·2958	1·14411	1·4981
2117	2·2984	1·14404	1·4982
2292	2·3007	1·14399	1·4982
2931	2·3084	1·14382	1·4982
3498	2·3160	1·14368	1·4983
4454	2·3291	1·14344	1·4984
5325	2·3407	1·14319	1·4984
5618	2·3448	1·14311	1·4984
6263	2·3544	1·14293	1·4985
10,342	2·4233	1·14185	1·4988

$\varepsilon = 2{\cdot}2741 + 10{\cdot}9w + 303w^2$
$v = 1{\cdot}14460 - 0{\cdot}265w$
$n_D^2 = 2{\cdot}2440 + 0{\cdot}216w$
$P = 312{\cdot}4$ c.c., $[R_D] = 40{\cdot}4$ c.c.
$\mu = 3{\cdot}65$ D.

	Acetyl-o-toluidine		
1380	2·2888	1·14428	—
2281	2·2983	1·14405	—
4136	2·3194	1·14365	—
4868	2·3306	1·14345	—

$\varepsilon = 2{\cdot}2741 + 10{\cdot}20w + 250w^2$
$v = 1{\cdot}14460 - 0{\cdot}234w$
$P = 326{\cdot}2$ c.c.
If $[R_D] = 45{\cdot}2$ c.c., $\mu = 3{\cdot}71$ D.

	Acetyl-α-naphthylamine		
1443	2·2865	1·14414	1·4981
2720	2·2969	1·14373	1·4982
3752	2·3061	1·14338	$1{\cdot}4983_5$
4318	2·3111	1·14323	1·4984

$\varepsilon = 2{\cdot}2741 + 8{\cdot}17w + 93w^2$
$v = 1{\cdot}14460 - 0{\cdot}320w$
$n_D^2 = 2{\cdot}2440 + 0{\cdot}28w$
$P = 330{\cdot}0$ c.c., $[R_D] = 54{\cdot}6$ c.c.
$\mu = 3{\cdot}67$ D.

	Acetyl-p-toluidine		
1021	2·2847	1·14434	—
1061	2·2856	1·14433	1·4981
2521	2·3003	1·14396	1·4982
2566	2·3012	1·14395	1·4982
3200	2·3084	1·14378	1·4982
4054	2·3176	1·14357	1·4983
4158	2·3190	1·14355	1·4983

$\varepsilon = 2{\cdot}2741 + 10{\cdot}40w + 100w^2$
$v = 1{\cdot}14460 - 0{\cdot}253w$
$n_D^2 = 2{\cdot}2440 + 0{\cdot}22w$
$P = 331{\cdot}3$ c.c., $[R_D] = 45{\cdot}2$ c.c.
$\mu = 3{\cdot}74$ D.

10^4w	ε	v	n_D
	*Acetyl-*m*-toluidine*		
1570	2·2901	1·14426	—
2110	2·2957	1·14414	1·4981
2453	2·2991	1·14408	1·4981
3324	2·3089	1·14389	1·4982
6270	2·3409	1·14328	1·4983
6920	2·3478	1·14316	1·4983
9828	2·3812	1·14257	1·4985

$\varepsilon = 2{\cdot}2741 + 10{\cdot}06w + 86w^2$
$v = 1{\cdot}14460 - 0{\cdot}210w$
$n_D^2 = 2{\cdot}2440 + 0{\cdot}153w$
$P = 323{\cdot}7$ c.c., $[R_D] = 45{\cdot}2$ c.c.
$\mu = 3{\cdot}69$ D.

	Acetyl-β-naphthylamine		
1353	2·2855	1·14416	—
2585	2·2962	1·14377	—
4003	2·3091	1·14333	—
5480	2·3232	1·14285	—

$\varepsilon = 2{\cdot}2741 + 8{\cdot}20w + 135w^2$
$v = 1{\cdot}14460 - 0{\cdot}319w$
$P = 331{\cdot}1$ c.c.
If $[R_D] = 54{\cdot}4$ c.c., $\mu = 3{\cdot}68$ D

	p-*Chloroacetanilide*		
649	2·2824	1·14435	$1{\cdot}4980_5$
773	2·2836	1·14430	1·4981
1196	2·2886	1·14414	$1{\cdot}4981_5$
1653	2·2940	1·14396	1·4982

$\varepsilon = 2{\cdot}2741 + 12{\cdot}2w$
$v = 1{\cdot}14460 - 0{\cdot}387w$
$n_D^2 = 2{\cdot}2440 + 0{\cdot}35w$
$P = 427{\cdot}3$; $[R_D] = 45{\cdot}2$ c.c.
$\mu = 4{\cdot}32$ D.

	Acetylaminodurene		
427	2·2777	1·14455	—
775	2·2807	1·14450	—
822	2·2811	1·14449	—
842	2·2813	1·14449	—

$\varepsilon = 2{\cdot}2741 + 8{\cdot}5w$
$v = 1{\cdot}14460 - 0{\cdot}13w$
$P = 363{\cdot}4$ c.c.
If $[R_D] = 59{\cdot}0$ c.c., $\mu = 3{\cdot}86$ D.

	p-*Bromoacetanilide*		
1076	2·2848	1·14411	$1{\cdot}4980_5$
2047	2·2943	1·14362	1·4981
3391	2·3075	1·14297	1·4982
4519	2·3186	1·14243	1·4983

$\varepsilon = 2{\cdot}2741 + 9{\cdot}83w$
$v = 1{\cdot}14460 - 0{\cdot}479w$
$n_D^2 = 2{\cdot}2440 + 0{\cdot}16w$
$P = 438{\cdot}3$ c.c.; $[R_D] = 48{\cdot}4$ c.c.
$\mu = 4{\cdot}36$ D.

Thanks are tendered to Imperial Chemical Industries Limited for a grant and for the loan of a precision variable condenser.

BEDFORD COLLEGE, REGENT'S PARK, LONDON, N.W.1. [*Received, February 24th*, 1961.]

929. *Some Condensation Products of Malononitrile.*

By D. M. W. Anderson, F. Bell, and J. L. Duncan.

Malononitrile has been condensed with a variety of carbonyl compounds, and the infrared spectra of the products are recorded.

Ostling [1] obtained a compound, $C_{15}H_{14}N_6$, volatile above 400°, by the interaction of acetone with a molecular amount of malononitrile in the presence of piperidine. Under the same conditions, but using a large excess of acetone, he obtained crystals, m. p. 175—180°, but analytical difficulties prevented assignment of an empirical formula. Schenck and Finken [2] by the condensation of acetone with malononitrile in the presence of potassium ethoxide obtained a compound, m. p. 171·5° (with gas evolution at a slightly higher temperature), which they regarded as isopropylidenemalononitrile (I). Cope and Hoyle [3] found, however, that isopropylidenemalononitrile is a liquid which can be readily converted into a dimer; they regarded this dimer as identical with Schenck and Finken's compound, and claim that the molecular weight determinations made by the latter authors, and which had indicated a monomer, must have been in error. Prout [4] has verified Cope and Hoyle's description of isopropylidenemalononitrile. All these experiments have now been repeated with somewhat conflicting results.

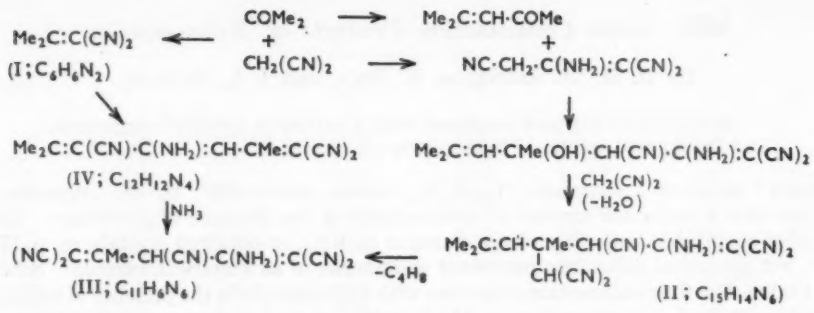
It is verified that the liquid isopropylidenemalononitrile is readily prepared by Cope and Hoyle's method but it is accompanied by a non-volatile pale yellow product, which undergoes indefinite decomposition above 300°. Schenck and Finken's method gives mainly a potassium salt which, after decomposition by acetic acid and crystallisation, yields colourless prisms or plates. These rapidly decompose at about 170° with evolution of isobutene and leave a pale yellow residue, which undergoes indefinite decomposition above 300°, and is very sparingly soluble in all common solvents. The same change can be brought about by dissolving the material in boiling acetic acid; the initially clear solution rapidly deposits the vary sparingly soluble decomposition product. Both of these compounds are readily soluble in aqueous ammonia and can be recovered by addition of acetic acid. Their relationship appears to be expressed by the equation $C_{15}H_{14}N_6 - C_4H_8 = C_{11}H_6N_6$. Since the C_{15} compound can be obtained by the condensation of mesityl oxide with malononitrile it appears probable that the readily expelled isobutene arises from the $Me_2C{:}CH$ group.

Ostling's second method gave crystals, m. p. 171—174°, which could be recrystallised from boiling acetic acid without change. This compound, which was identical with Cope and Hoyle's dimer, is sparingly soluble in aqueous ammonia in the cold but on boiling slowly dissolves with elimination of acetone. On acidification of this solution there is precipitated the compound of decomposition point >300°.

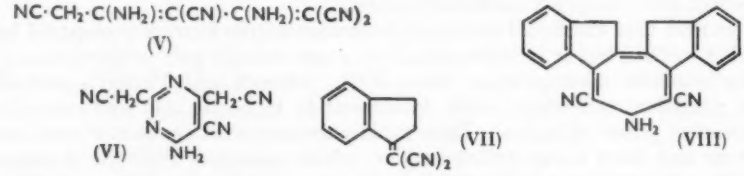
In the polymerisation of isopropylidenemalononitrile very slight changes in conditions determine whether there is produced Cope and Hoyle's dimer or Schenck and Finken's compound. If aqueous ammonia is used to bring about the condensation of malononitrile with acetone, the compound of decomposition point >300° is produced together with a trimer of malononitrile. The two are somewhat similar in properties but malononitrile trimer is sparingly soluble in aqueous ammonia, and can be sublimed without decomposition, whereas the acetone condensation product when heated slowly decomposes with only slight sublimation of product.

The infrared spectra suggest that the acetone–malononitrile reaction may follow the course:

[1] Ostling, *Chem. Zentr.*, 1921, **1**, 613.
[2] Schenck and Finken, *Annalen*, 1928, **462**, 273.
[3] Cope and Hoyle, *J. Amer. Chem. Soc.*, 1941, **63**, 733.
[4] Prout, *J. Org. Chem.*, 1953, **18**, 928.

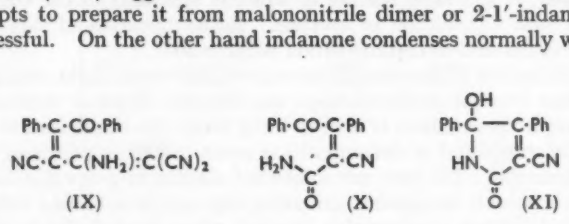


Schenck and Finken described two, possibly three, forms of malononitrile trimer. Their experiments have been repeated, and infrared examination shows only two distinct modifications, one of which is vigorously transformed into the other at 230°. The stable form has a spectrum most readily interpreted as that of an unsaturated aliphatic compound (V); the spectrum of the less stable form strongly suggests a ring structure such as (VI), although this suggestion is difficult to accept chemically.



Benzophenone and fluorenone condense with malononitrile to yield uniform products already described,[2] analogous to (I). Mowry [5] described the preparation of $PhMeC{:}C(CN)_2$ from acetophenone and malononitrile. It is now found that slightly more vigorous conditions result in the production of a yellow isomer with an as yet unexplained infrared spectrum.

The interaction of malononitrile with indanone is complex. Compound (VII) is obtained by boiling the components in pyridine, or in ethanol containing piperidine. Use of potassium carbonate produces an orange compound, m. p. 250°, whose formation appears to be represented by the equation $2C_9H_8O + 2C_3H_2N_2 - HCN - 2H_2O = C_{33}H_{15}N_3$; structure (VIII) suggested for this does not conflict with the infrared evidence. However, attempts to prepare it from malononitrile dimer or 2-1′-indanylideneindan-1-one were unsuccessful. On the other hand indanone condenses normally with cyanoacetic esters.[6]



Benzoin condensed with malononitrile to give a compound of type (I), but benzil gave material to which structure (IX) is assigned. The condensation of benzil with cyanoacetamide occurred in 1 : 1 ratio but the infrared spectrum suggested that the product is (XI) rather than (X). Bacher's results [7] with ethyl cyanoacetate were verified in that

[5] Mowry, U.S.P. 2,458,017 (1949).
[6] Ingold and Thorpe, *J.*, 1919, **115**, 150.
[7] Bacher, *J. prakt. Chem.*, 1929, [2], **120**, 323.

two compounds were obtained but the infrared spectrum of the higher-melting compound did not correspond to the structure assigned by Bacher.

Various derivatives of isatin were examined and all the products proved to be of type (I). Acenaphthenequinone and phenanthraquinone both reacted readily with malononitrile in the presence of potassium carbonate to give coloured products. Neither product was obtained sufficiently pure for an empirical formula to be suggested.

Sachs [8] described a series of condensation products of nitriles with nitrosophenols. We examined the interaction of various nitrosophenols with malononitrile but obtained only black, amorphous solids, which resisted purification. Most of the other compounds described by Sachs were similar and the only clearly defined one was *N*-α-cyanobenzylidene-*p*-hydroxyaniline, from benzyl cyanide. Too long contact of this with the sodium hydroxide used as condensing agent resulted in its complete conversion into *p*-hydroxybenzanilide.

Experimental

Infrared spectra were determined as Nujol and hexachlorobutadiene mulls with a Hilger H 800 spectrophotometer. Where indicated, spectra were also obtained as dilute solutions (0·01M) in methylene dichloride. Results are recorded in cm.$^{-1}$.

Acetone and Malononitrile.—(*a*) Isopropylidenemalononitrile (I), b. p. 98°/10 mm., was prepared by the method of Cope and Hoyle.[3] The residue from the distillation formed, after removal of more soluble material by ethanol, a pale yellow powder, decomp. >300°, sparingly soluble in the usual organic solvents. It was easily soluble in aqueous ammonia from which it could be reprecipitated by addition of acetic acid (Found: C, 59·3; H, 3·2%), and was identical with the compound described under (*b*).

(*b*) Interaction of acetone with malononitrile under the conditions given by Schenck and Finken yielded a pale yellow potassium salt. Decomposition of this by acetic acid gave a product fairly soluble in acetone. Dilution of the hot acetone solution led to the formation of plates [Found: C, 64·6, 64·6; H, 5·2, 5·0; N, 29·7, 29·1. $C_{15}H_{14}N_6$ (II) requires C, 64·7; H, 5·0; N, 30·2%], which underwent vigorous disintegration at *ca.* 170° with evolution of isobutene (loss in weight; 19·7, 20·0. $C_{15}H_{14}N_6 \longrightarrow C_{11}H_6N_6$ requires loss, 20·1%; isobutene identified by infrared spectrum) to yield a pale yellow powder of indefinite decomp. >300° (Found: C, 59·3, 60·3; H, 3·3, 3·1; N, 36·5. $C_{11}H_6N_6$ requires C, 59·4; H, 2·7; N, 37·8%). The primary product is soluble in aqueous ammonia and can be recovered by addition of acetic acid; it is fairly soluble in acetic acid but if the solution is boiled the isobutene-free compound separates.

(*c*) Diethylamine (0·2 c.c.) in acetone (2 c.c.) was added to a cold solution of malononitrile (5 g.) in acetone (25 c.c.). The mixture immediately became very hot. . Next day the crystals, m. p. 170—174°, were removed (2·4 g.) and recrystallised from ethanol, giving isopropylidenemalononitrile dimer (IV)[3] as prisms, m. p. 171—174° (Found: C, 67·8; H, 5·9. Calc. for $C_{12}H_{12}N_4$: C, 67·9; H, 5·7%). This compound can be recrystallised from boiling acetic acid without change. It is slowly soluble in cold aqueous ammonia but on boiling passes into solution from which acetic acid precipitates the compound of high decomp. point described under (*b*); the solution contains acetone, which was identified as the 2,4-dinitrophenylhydrazone.

If in this experiment the concentration of the malononitrile is raised (*e.g.*, 5 g. in 10 c.c. of acetone) the principal product is no longer the dimer but the compound, decomp. 170°, described under (*b*).

(*d*) Diethylamine (0·2 c.c.) in ethanol (2 c.c.) was added to a mixture of mesityl oxide (3 c.c.) and malononitrile (1·7 g.) in ethanol (5 c.c.), and the whole was kept at about 70° for 2 hr. Almost colourless prisms were deposited (1·1 g.), identical with the compound, decomp. 170°, described under (*b*). Further crops were less pure. If in this experiment the ethanol is omitted there is obtained the compound, decomp. >300°.

(*e*) Isopropylidenemalononitrile was treated (i) with piperidine or (ii) in benzene solution with piperidine, or (iii) in acetone solution with diethylamine. In each case the product disintegrated at *ca.* 170° [*i.e.*, it was identical with the compound described under (*b*) and not with the dimer described under (*c*); cf. ref. 3].

[8] Sachs, D.R.-P., 121, 974.

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(*f*) Mesityl oxide did not react with malononitrile under the conditions used to prepare isopropylidenemalononitrile. No condensation product was isolated from a mixture of phorone and malononitrile containing diethylamine.

(*g*) No reaction occurred between malononitrile dimer and acetone in the presence of diethylamine. Attempted condensation in ethanol by potassium ethoxide also failed.

(*h*) When aqueous ammonia was added to a solution of malononitrile (3 g.) in acetone (5 c.c.) the whole became very hot and in a few minutes had set to a yellow crystalline mass. After acidification with hydrochloric acid the precipitate proved to be essentially compound (III). A further deposit consisted of malononitrile trimer, which could be purified by sublimation.

TABLE 1.

Infrared spectra of products from acetone and malononitrile.

Compound	NH_2 stretch	CN	NH_2 bend	C:C	CMe_2
(I)	—	2260w	—	1610s	1390s
		2230s			1373s
(II)	3480m	2260vw	1660s	1612s	1395m
	3330m	2230s		1585s	1372s
		2220s			
(III)	3340m	2220s	1660s	1620m	—
	3230w	2210s		1595s	
(IV)	3390m	2235w	1646s	1570s	1385s
	3290m	2208s			1370s
	3190m				

Polymers of Malononitrile.—(*a*) Schenck and Finken's [2] "malononitrile trimer-(II)" prepared by the action of dry ammonia on a benzene suspension of malononitrile, was crystallised from a little ethanol, and the product boiled with ethyl acetate to remove coloured impurities. The residue had m. p. 220—224° (Found: C, 54·6; H, 3·5; N, 42·2. Calc. for $C_9H_6N_6$: C, 54·3; H, 3·0; N, 42·4%). Its infrared absorptions (see Table 2) indicate a structure such as (VI).

(*b*) When malononitrile trimer was heated in a bath to about 230° violent change occurred. The residual dark mass was extracted with boiling pyridine and the extract diluted with ethanol. The product, which darkened slightly above 300° but was unmelted at 360°, could be obtained as pale yellow crystals from boiling formic acid. This corresponds to Schenck and Finken's trimer-III (Found: C, 54·9; H, 3·3%).

(*c*) Malononitrile (1 g.) was added to diethylamine (~1 c.c.). The solution became very hot. After a short time excess of dilute hydrochloric acid was added and the precipitated thick oil solidified on boiling with ethanol. The product, on crystallisation from water, gave malononitrile dimer as needles, m. p. 168—170°.

(*d*) Submission of malononitrile to Schenck and Fincken's process for the preparation of trimer-I gave only the dimer, m. p. 170°. The dimer when heated above 200° underwent a complex decomposition and no definite compound could be isolated from the product.

TABLE 2.

Infrared spectra of malononitrile trimers.

Schenck and Finken designation	NH stretch.	CN	C:C	Other bonds
Trimer-II	3220m, broad bonded NH	2260w 2210s	—	1535s, 1510s 1432s, 1415s (Pyrimidine ring?)
Trimer-III	3410m, 3340m . 3250m, 3175m	2275w 2230s	1595s 1550s	—

Acetophenone and Malononitrile.—A mixture of acetophenone (4 c.c.) and malononitrile (2 g.) containing a few drops of diethylamine was kept warm for a few hr. and allowed to cool. The semisolid product was treated with ethanol to remove more soluble material and the residue, m. p. 120—130°, fractionally crystallised from acetic acid to yield colourless needles of 1,1-dicyano-2-methyl-2-phenylethylene, m. p. 94° (also obtained in good yield by Mowry's method [5]), and canary-yellow needles of an *isomer*, m. p. 205—207° (Found: C, 78·5; H, 4·8. $C_{11}H_8N_2$ requires C, 78·6; H, 4·8%). The compound of low m. p. could be partially converted into the yellow compound by heating it at about 70° for 3 hr. in the presence of a small amount of diethylamine. The infrared spectrum of the yellow compound did not agree with the

TABLE 3.

Infrared spectra of products from acetophenone and malononitrile.

Compound	NH	CN	Ph	C=C	CMe	Ph
M. p. 94°	—	2235m	1598w 1587m 1492m	1568m	1439m 1374m	772s 760s
M. p. 205—207°	3240m	2220m 2205m	1578m 1490w 1457w	1603vs	—	763s, 741s 699s, 694s

expected 4-amino-1,1,5-tricyano-2,6-diphenylhepta-1,3,5-triene. The NH absorption was checked in solution (methylene dichloride).

Ethyl α-cyano-1-indanylideneacetate, prepared by Ingold and Thorpe's method,[9] formed needles, m. p. 100—102°; ν 2234w (CN), 1718s (ester C=O), and 1570s (C=C). The *methyl* ester, prepared similarly, crystallised from methanol as needles, m. p. 142—144° (Found: C, 73·5; H, 4·9. $C_{13}H_{11}O_2N$ requires C, 73·3; H, 5·2%); ν 2235vw (CN), 1728s (ester C=O), 1575s (C:C).

1-*Indanone and Malononitrile.*—(*a*) 1-*Dicyanomethyleneindane*, prepared by boiling indanone and malononitrile either in pyridine or in ethanol containing one drop of piperidine, crystallised from ethanol in needles, m. p. 152° (Found: C, 80·1; H, 4·5. $C_{12}H_8N_2$ requires C, 80·0; H, 4·5%); ν 2236w (CN), 1575m (C:C). 2-1′-Indanylideneindan-1-one was unchanged after boiling with malononitrile, malononitrile dimer, or ethyl cyanoacetate in ethanol even in the presence of piperidine or potassium carbonate; it shows the following infrared bands: 1655s (αβ-unsaturated ketone), 1615w (C:C).

(*b*) Potassium carbonate (3 g.) was added to a mixture of 1-indanone (2 g.) and malononitrile (1·5 g.) in ethanol and the whole warmed on a steam bath for 10 min. and cooled. Water was added and the precipitate filtered off; from this the more soluble material was removed by boiling ethanol. The residue yielded from pyridine–ethanol a *compound* as yellow prisms, m. p. *ca.* 250° (Found: C, 82·2; H, 4·6; N, 12·6. $C_{33}H_{15}N_3$ requires C, 82·9; H, 4·5; N, 12·6%); ν 3390, 3330, 3240, 2228 (all m), 2190s, 1655s, 1617m, 1595m, 1537m. The analyses and spectrum suggest a structure such as (VIII).

(*c*) Potassium carbonate (2·5 g.) was added to a boiling solution of indanone (1·3 g.) and 1-dicyanomethyleneindane (1·8 g.) in ethanol (40 c.c.) and the boiling continued for ½ hr. Water was then added and a small amount of precipitated 1-dicyanomethyleneindane filtered off. The filtrate was acidified with acetic acid and the precipitated plastic mass recrystallised from acetic acid. A *compound* was obtained as almost colourless needles, m. p. 250—255° to a deep-green melt (Found: C, 80·6; H, 5·1; N, 8·8. $C_{21}H_{14}N_2O$ requires C, 80·7; H, 5·1; N, 9·0%); ν 3420m, 3350m, 3200w, 2200s, 1715s, 1655m, 1635m, 1590m, 1575m.

Fluorenone and Malononitrile.—Fluorenylidenemalononitrile crystallised from acetic acid in red needles, m. p. 234—235° (lit., m. p. 213°,[2] 234° [11]); ν 2225, 1615, 1575, 1562 (all m).

Benzophenone and Malononitrile.—1,1-Dicyano-2,2-diphenylethylene crystallised from ethanol in needles, m. p. 138° (lit.[2] m. p. 136°); ν 2225m (CN), 1530m (C:C).

Benzoin and Malononitrile.—A few drops of diethylamine were added to a hot solution of benzoin (2·1 g.) and malononitrile (1·4 g.) in ethanol (20 c.c.), and the mixture kept warm for 2 hr. On cooling, benzil (0·7 g.) separated. The filtrate was re-heated and diluted. The resultant crop was recrystallised from ethanol to yield almost colourless needles, m. p. 204—206° (Found: C, 78·1; H, 4·5; N, 10·9. $C_{17}H_{12}N_2O$ requires C, 78·5; H, 4·6; N, 10·8%); ν 3450, 3315, 3260, 3200 (all m) (OH), 2235s, (CN), and 1658s (C=C).

Benzil and Malononitrile.—Diethylaniline (0·2 c.c.) was added to a warm solution of benzil (2·1 g.) and malononitrile (1·4 g.) in ethanol (25 c.c.), and the mixture kept at 70° for 2 hr. On slight dilution needles separated, m. p. *ca.* 120° with evolution of ethanol (Found: C, 71·6; H, 5·1; loss at 130°, 12·6%. $C_{20}H_{12}N_4O,C_2H_5OH$ requires C, 71·4; H, 4·9; loss, 12·4%). The residue of 2-*amino*-4-*benzoyl*-1,1,3-*tricyano*-4-*phenylbutadiene* had m. p. *ca.* 195° (decomp.) (Found: C, 73·8; H, 4·1; N, 17·3. $C_{20}H_{12}N_4O$ requires C, 74·1; H, 3·7; N, 17·3%); ν 3390m, 3310m (NH_2), 2240w (CN), 1740sh, 1722s (C=O). The ethanolate gave the same spectrum

[9] Walter, *Ber.*, 1902, **35**, 1321.
[10] Corson and Stoughton, *J. Amer. Chem. Soc.*, 1928, **50**, 2825.
[11] Ferrier and Campbell, *J.*, 1960, 3514.

with additional bands at 3520m and 1042m due to ethanol. Similar addition compounds were obtained with other alcohols.

Benzil and Ethyl Cyanoacetate.—Condensation by Bacher's method[7] led to the two compounds described by him. One, prisms, m. p. 139—141° (Found: C, 74·7; H, 5·1. Calc. for $C_{19}H_{15}NO_3$: C, 74·7; H, 4·9%), gave the infrared spectrum expected for ethyl α-cyano-β-benzoylcinnamate: 2240w (CN), 1727s (ester C:O), and 1669s (keto-C:O). The other, prisms, m. p. 169—171° (Found: C, 69·0; H, 5·1. Calc. for $C_{24}H_{22}N_2O_5$: C, 68·9; H, 5·3%) did not give the spectrum expected for ethyl αγ-dicyano-β-phenyl-β-benzoylglutarate but gave evidence of the presence of an NH group. The main bands shown were 3180m broad (NH), 2250vw (CN), 1743s (ester C:O), and 1691s (keto-C:O).

Benzil and Cyanoacetamide.—A few drops of diethylamine were added to a hot solution of benzil (2·1 g.) and cyanoacetamide (1·7 g.) in ethanol (40 c.c.). Next day water was added and the precipitate crystallised from aqueous ethanol, giving prismatic needles, m. p. 167—170° (Found: C, 71·3; H, 4·5; N, 9·5. $C_{17}H_{12}N_2O_2,\frac{1}{2}H_2O$ requires C, 71·5; H, 4·6; N, 9·8%), or from xylene as needles, m. p. 180—182° (Found: C, 74·3; H, 4·3. $C_{17}H_{12}N_2O_2$ requires C, 73·9; H, 4·3%); ν 3300s, 1348s, 1176s (bonded −OH), 3250m (NH), 2230m (CN), 1715s (C:O), in better agreement with formula (VIII) than with (VII).

Derivatives of Oxindole.—(*a*) 3-Dicyanomethyleneoxindole was prepared by Walter's method. When boiled for 1 hr. with acetic anhydride it gave the N-*acetyl derivative* as dichromate-coloured needles, m. p. 170° (Found: C, 65·9; H, 2·9. $C_{13}H_7N_3O_2$ requires C, 65·8; H, 2·9%).

(*b*) *Methyl α-cyano-3-oxindolylideneacetate*, prepared by the addition of anhydrous potassium carbonate (2 g.) to a boiling suspension of isatin (1 g.) in methanol (10 c.c.) containing methyl cyanoacetate (1 c.c.), crystallised from acetic acid in needles, m. p. 240—242° (decomp.) (Found: C, 63·4; H, 3·6. $C_{12}H_8N_2O_3$ requires C, 63·2; H, 3·5%). When boiled with acetic anhydride it gave the N-*acetyl derivative* as bright yellow crystals, m. p. 147—149° (Found: C, 62·0; H, 3·9. $C_{14}H_{10}N_2O_4$ requires C, 62·2; H, 3·7%).

(*c*) *5-Methyl-3-dicyanomethyleneoxindole* was formed immediately on addition of malononitrile to a boiling ethanolic solution of 5-methylisatin. It crystallised from acetic acid as brownish violet needles, m. p. 260° (Found: C, 68·7; H, 2·9. $C_{12}H_7N_3O$ requires C, 68·9; H, 3·3%), and by solution in boiling acetic anhydride gave the *acetyl derivative*, which crystallised from acetic acid as red needles, m. p. 198—200° (Found: C, 67·1; H, 3·6; N, 16·4. $C_{14}H_9N_3O_2$ requires C, 66·9; H, 3·6; N, 16·7%).

(*d*) On boiling 5-methylisatin (1 g.) and malononitrile dimer (1 g.) in ethanol (20 c.c.) condensation occurred slowly to give red-violet crystals of *3-(2-amino-1,3,5-tricyanoallylidene)-5-methyloxindole*, m. p. 333° (decomp.) (Found: C, 65·4; H, 3·5. $C_{15}H_9N_5O$ requires C, 65·4; H, 3·3%).

TABLE 4.

Infrared spectra of oxindoles.

						C=O			
R¹	R²	R³	R⁵	NH	CN	keto	ester	acyl	C=C
H	CN	CN	H	{3290m 3160m	2245w	{1740s 1722s	—	—	1627m
				*3415m	2245w	1747s			1625m
Ac	CN	CN	H	—	2240w	1720s	—	—	1600m
H	CN	CO_2Me	H	3360m	2225w	1720s	{1755sh 1730s	—	1620m
				*3400m	2230w	1745s, (1 peak only)	—	—	1623m
Ac	CN	CO_2Me	H	—	2220w	1720s	1740s	1762s	1610m
H	CN	CN	Me	3280m	2240w	{1737s 1722s	—	—	1625m
				*3410m	2242w	1745s	—	—	1625m
Ac	CN	CN	Me	—	2235w	1725s	—	1755s	1603m

* In dichloromethane solution. Numerals attached to the R's refer to positions in the oxindole nucleus.

Acenaphthenequinone and Malononitrile.—Anhydrous potassium carbonate (3 g.) was added to a boiling mixture of acenaphthenequinone (2 g.) and malononitrile (2 g.) in ethanol (100 c.c.).

After ½ hr. the deep blue solution was diluted with hot water (100 c.c.) and allowed to cool. The product was filtered off, dried, and extracted (Soxhlet) with acetone. The blue-black product had a decomposition point >300° and contained potassium. The infrared spectrum showed extensive broad bands at 1520—1580, and 2200 (CN), but no carbonyl. Acenaphthenequinone did not condense with cyanoacetamide or ethyl cyanoacetate under the same conditions.

Phenanthraquinone and Malononitrile.—A few drops of diethylamine were added to a boiling solution of phenanthraquinone (1 g.) and malononitrile (1 g.) in ethanol (200 c.c.). The mixture immediately became deep-purple and deposited a dark-violet precipitate. This was filtered off, dried, and extracted (Soxhlet) with acetone. The almost black product decomposed at 300°, and showed infrared bands at 3270s, 2240s, 1650, 1612, 1592, 1550, and 1515 (all m).

p-*Nitrosophenol Series.*—*N*-α-Cyanobenzylidene-*p*-hydroxyaniline was prepared by Sachs's method.[8] Too long contact with the ethanolic solution of sodium hydroxide resulted in its conversion into *p*-hydroxybenzanilide, m. p. 214° (Found: C, 73·1; H, 5·0; N, 6·9. Calc. for $C_{13}H_{11}NO_2$: C, 73·3; H, 5·2; N, 6·6%).

By the same method 3-methyl-4-nitrosophenol gave *N*-α-cyanobenzylidene-4-hydroxy-2-methylaniline, which crystallised from ethanol as yellow needles, m. p. 198—200° (Found: C, 76·5; H, 5·0. $C_{15}H_{12}N_2O$ requires C, 76·3; H, 5·1%), and 2-methyl-4-nitrosophenol gave N-α-*cyanobenzylidene*-4-*hydroxy*-3-*methylaniline*, m. p. 142—144°, from ethanol (Found: C, 76·2; H, 4·6%).

TABLE 5.

Infrared spectra of 4-nitrosophenols, 4-HO·C_6H_3R·N:C(CN)Ph.

R	OH	CN	N:C
H	3323m	2220vw	1620m
2-Me	3320m	2220w	1620m
3-Me	3280m	2220vw	1622m

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930. *Chemical Constitution and Amœbicidal Activity. Part VI.* A New Synthesis of 2-Ketones and 2-Alcohols derived from 3-Alkyl-1,3,4,6,7,11b-hexahydro-9,10-dimethoxy-2H-benzo[a]quinolizines.*

By J. M. OSBOND.

Synthesis and cyclisation of the ketals (II; R = Et, Bu^n, and Bu^i) to the benzo[*a*]quinolizine derivatives (III and IV) are described. The reduction of these compounds by various reagents to the more saturated ketones (V) and alcohols (VII), and reconversion of the former by chloranil into the αβ-unsaturated ketones (IV), are reported. Dehydrogenation with mercuric acetate of the compounds (IV), (V), and (VII) has been investigated.

SEVERAL 2-ketones[1a,b] and 2-alcohols[1c] of the series 3-alkyl-1,3,4,6,7,11b-hexahydro-9,10-dimethoxy-2*H*-benzo[*a*]quinolizine (cf. V and VII) have been described and shown to have important psycho-sedative properties[2] and have provided the intermediate

* Part V, *J.*, 1959, 3630.

[1] (*a*) Brossi, Lindlar, Walter, and Schnider, *Helv. Chim. Acta*, 1958, **41**, 119; (*b*) Battersby, Openshaw, and Wood, *J.*, 1953, 2463; (*c*) Brossi, Chopard, and Schnider, *Helv. Chim. Acta*, 1958, **41**, 1793.

[2] Pletscher, *Science*, 1957, **126**, 507; Pletscher, Besendorf, and Bachtold, *Arch. exp. Path. Pharmakol.*, 1958, **232**, 499.

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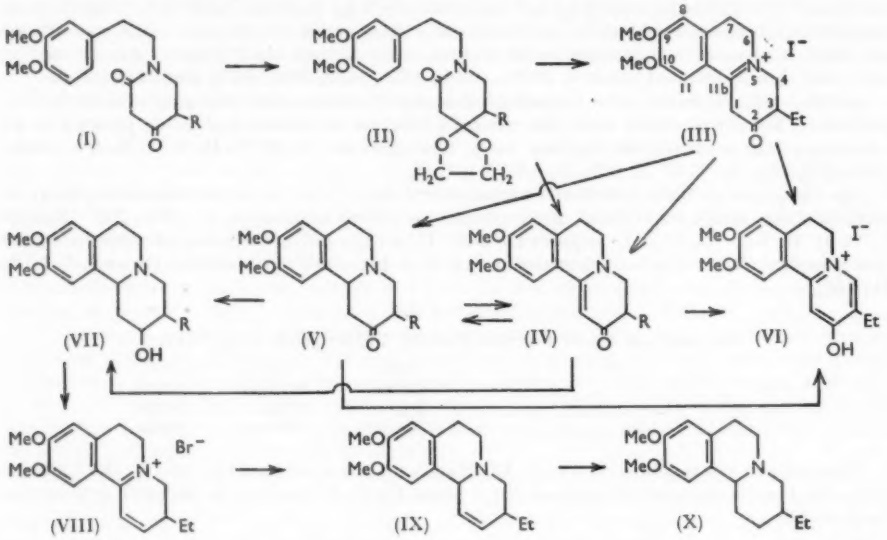
compounds for the synthesis of emetine,[3a] dehydroemetine,[3b] and their isomers and analogues.

A new route to this type of compound is now described and involves the cyclisation of the ketals (II; R = Et, Bu^n, or Bu^i). Synthesis of the phenethylpiperidinedione (I; R = Et) and its ketal (II) was recorded first by Ban;[4a] both compounds have now

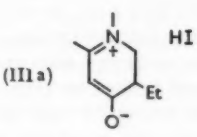


been obtained crystalline.[4b] In a similar way, *via* the Mannich base from 3,4-dimethoxyphenethylamine, formaldehyde, and a substituted malonic acid, we have prepared the compounds (I; R = Bu^n and Bu^i) and the corresponding ketals (II). An attempt by Ban[4a] to cyclise the ethyl compound (II; R = Et) with phosphorus oxychloride was unsuccessful; after our work[5] had been completed, Itoh and Sugasawa[6] effected this cyclisation with phosphorus pentoxide, obtaining a benzo[*a*]quinolizinium salt. In our hands, treatment with phosphorus oxychloride in toluene gave, after brief acid hydrolysis and addition of potassium iodide, a quaternary iodide (III) in 73% yield.

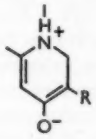
Treatment of this iodide (III) with sodium hydroxide gave the yellow base (IV; R = Et) which was characterised as hydrochloride, hydrobromide, and hydriodide which on basification regenerated the same base. From the ultraviolet absorption spectra in ethanol or water it appeared that the base (IV; R = Et) and its salts had similar structures (see Table, nos. 2—4) but were different from the quaternary iodide (III) (no. 1). Indeed the hydriodide and quaternary iodide differed in melting point, infrared and ultraviolet spectra, and chemical reactions (see below). Conversion of the quaternary iodide into the non-crystalline chloride and treatment of this with 48% hydrobromic acid also gave the hydrobromide of base (IV; R = Et). The greater stability of the tertiary (IV) than of the quaternary structure (III) was also illustrated by the cyclisation of the ketals (II; R = Bu^n and Bu^i). Several attempts to isolate structures corresponding to (III) were made but only salts of the tertiary type (IV) were isolated and attempts to convert these into the quaternary derivatives (III; R = Bu^n or Bu^i) under various conditions

[3] (*a*) Brossi, Baumann, and Schnider, *Helv. Chim. Acta*, 1959, **42**, 1515; (*b*) Brossi, Baumann, Chopard, Würsch, Schneider, and Schnider, *ibid.*, 1959, **42**, 772; Osbond, B.P. Spec. 835,489.
[4] (*a*) Ban, *Pharm. Bull.* (*Japan*), 1955, **3**, 53; (*b*) Barash, Osbond, and Wickens, *J.*, 1959, 3530.
[5] Osbond, B.P. Spec. 861,524, (1957), 861,525 (1957).
[6] Itoh and Sugasawa, *J. Org. Chem.*, 1959, **24**, 2042.

were unsuccessful. This behaviour is unusual in the sense that normally enamines with acid give the immonium salt;[7] presumably in this case the keto-group stabilises the structure (IV). Nevertheless, although the ultraviolet absorption of the bases (IV; R = Et, Bu^n, and Bu^i) and their salts in ethanol and water (Table; compare nos. 1, 7, and 9 with 3, 4, 6, and 10) differed from that of the quaternary salt (III), yet in dilute acid these salts all had ultraviolet absorption similar to that of the quaternary iodide (III) in water (compare nos. 5, 8, 11, and 12 with 1). The structure of the quaternary iodide (III) and



(IIIa)



(IVa)

the bases (IV) could probably be more accurately formulated as polar forms such as (IIIa) and (IVa) on the basis of their ultraviolet and infrared spectra. The ultraviolet spectrum of salt (III) shows a more complex chromophoric system than is present in the simple 1,2,3,4,6,7-hexahydrobenzo[*a*]quinolizinium compounds,[8] and the infrared spectrum shows no hydroxyl band and a ketone band at 1630 cm.$^{-1}$ (for $\nu_{max.}$ of this and other compounds see the Experimental section). Similarly the bases and salts (IV; R = Et and Bu^i) showed no hydroxyl band; the bases had only weak bands in the carbonyl region (1640—1698 cm.$^{-1}$), and the salts showed bands of medium intensity at ~1635 cm.$^{-1}$ (cf. infrared spectrum of 4-hydroxypyridine;[9] C=O band at 1638 cm.$^{-1}$).

The iodide (III) undergoes two reactions not given by the bases (IV; R = Et, Bu^n, or Bu^i) or their salts: (1) The melting point of the quaternary iodide [III; m. p. 171—172·5°, followed by resolidification at ~180° and finally melting at 240—241° (decomp.)] was interpreted as due to aromatisation of the heterocyclic ring by disproportionation;

Ultraviolet absorption spectra.

No.	Compound	Solvent	$\lambda_{max.}$ (mμ)	log ε
1	(III)	H_2O	225, 249, 330—335	4·26, 4·06, 4·22
2	(IV; R = Et)	EtOH	237, 284, 360—363	4·33, 3·96, 4·30
3	(IV; R = Et), HCl	H_2O	239, 288, 360	4·28, 3·89, 4·27
4	(IV; R = Et), HBr	H_2O	237·5, 288, 360	4·30, 3·91, 4·26
5	(IV; R = Et), HCl	0·2N-HCl	250, 341	4·15, 4·31
6	(IV; R = Et), HI	H_2O	232, 288, 360	4·39, 3·86, 4·24
7	(IV; R = Bu^n)	EtOH	237, 286, 361—362	4·26, 3·90, 4·14
8	(IV; R = Bu^n), HBr	0·2N-HCl	250, 335	4·20, 4·30
9	(IV; R = Bu^i)	EtOH	238, 284—285, 362	4·29, 3·91, 4·23
10	(IV; R = Bu^i), HI	H_2O	229—230, 282—283, 360	4·40, 3·93, 4·21
11	(IV; R = Bu^i), HBr	0·2N-HCl	250, 335	4·22, 4·30
12	(IV; R = Bu^i), HCl	0·2N-HCl	250, 340	4·18, 4·29
13	(V; R = Et), HCl	H_2O	225, 282	3·94, 3·9
14	(VI)	H_2O	230, 260, 312	4·48, 4·39, 4·20
15	(VIII)	H_2O	277, 355	4·27, 4·23
16	(VIII)	0·1N-NaOH	277, 355	4·20, 4·16
17	(IX)	H_2O	226, 282	3·87, 3·56

thus pyrolysis of this salt at 180° gave 3-ethyl-6,7-dihydro-2-hydroxy-9,10-dimethoxybenzo[*a*]quinolizinium iodide (VI) whose structure was confirmed by the ultraviolet absorption spectrum (no. 14; cf. the bromide [1a]) and by conversion into the pyridone form (m. p. 227—230°), identical with an authentic specimen [1a] (see below). By contrast, the hydriodide of the base (IV; R = Et) was thermally stable, although treatment of

[7] Leonard and Gash, *J. Amer. Chem. Soc.*, 1954, **76**, 2781; Witkop, *ibid.*, 1956, **78**, 2873.
[8] Ban and Yonemitsu, *Chem. and Pharm. Bull. (Japan)*, 1960, **8**, 653.
[9] Mason, *J.*, 1957, 4874.

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the base with mercuric acetate [10,1a] readily gave the salt (as VI). (2) Potassium borohydride [11] reduced the salt (III) in methanol to ketone (V; R = Et), rapidly and in 94% yield. Comparison, by mixed melting point and infrared spectra, of this product and its hydrochloride and hydrobromide with authentic specimens [1a] showed them to be identical. By contrast, similar attempts to reduce the bases (IV; R = Et, Bu^n, or Bu^i) and their salts under a variety of conditions failed, only unchanged material being obtained. This ready reduction of the salt (III) supports the immonium structure proposed for this iodide (cf. ref. 11).

Reduction of the bases (IV; R = Et, Bu^n, and Bu^i) was, however, effected by three reagents: (1) Lithium aluminium hydride in boiling tetrahydrofuran gave the saturated ketones in fair yield. The retention of the ketone group was unexpected; selective reduction of the double bond of an αβ-unsaturated ketone or ester is rare [12a] although complete reduction to the saturated alcohol is well known.[12b] (2) Reduction of the base (IV; R = Et) with lithium [13] in ammonia also gave the saturated ketone (V; R = Et) in 30% yield. (3) The same base in presence of palladised charcoal absorbed 2 mol. of hydrogen, giving the alcohol (VII; R = Et), identical with a specimen obtained from ketone (V; R = Et) by hydrogenation [1b] with Adams catalyst.

Dehydrogenation of the αβ-saturated ketones (V; R = Et, Bu^n, and Bu^i) has been effected with two reagents. (1) It was hoped that treatment of the ethyl derivative with a limited quantity of mercuric acetate would give the unsaturated ketone (IV). However, treatment with one mol. gave only unchanged starting material, and use of 2 mol. gave a 60% yield of the quaternary bromide (VI) together with mercury but no mercurous acetate. (2) Chloranil [14] in benzene, however, readily dehydrogenated all three ketones (V) to their unsaturated derivatives (IV) in good yield. In the butyl case, the primary product was a 2 : 1 adduct [15] of ketone (IV; R = Bu^n) and tetrachloroquinol that appeared to be stable to base but with acid gave the required salt of (IV).

The alcohol (VII; R = Et) with mercuric acetate (2 mol.) gave the quaternary salt (VIII) in 30% yield, mercurous acetate, and a little mercury. With an excess of the reagent the yield of salt (VIII) was 92%. This formulation (enamine) was based on analysis and the ultraviolet absorption spectrum (Table, no. 15); in 0·1N-sodium hydroxide the maxima were unchanged (no. 16) and this suggests the alternative arrangement of double bonds (enamine form) for (VIII). However, the ready reduction of this product by potassium borohydride to the base (IX) (the spectrum of which shows only the dimethoxybenzene chromophore) supports structure (VIII). The presence of one isolated double bond was proved by hydrogenation of product (IX) with Adams catalyst (1 mol. absorbed) to 3-ethyl-1,3,4,6,7,11*b*-hexahydro-9,10-dimethoxy-2*H*-benzo[*a*]quinolizine (X).

Experimental

Spectroscopic data for compounds marked * are shown in Table 1. The infrared spectra were determined for Nujol mulls by Dr. A. Wagland.

Butyl-3,4-dimethoxyphenethylaminomethylmalonic Acid.—To a solution of 3,4-dimethoxyphenethylamine (163 g.) and n-butylmalonic acid (160·5 g.) in ethanol (500 c.c.) and water (1050 c.c.), 40% aqueous formaldehyde (121 c.c.) was added at 0°. After 16 hr. at 0° the *acid* (247 g.) was filtered off, dried, and washed with hot ethanol; it had m. p. 150° (decomp.) (Found: C, 60·7; H, 7·8; N, 3·8. $C_{18}H_{27}NO_6$ requires C, 61·2; H, 7·7; N, 4·0%).

[10] Leonard, Hay, Fulmer, and Gash, *J. Amer. Chem. Soc.*, 1955, **77**, 439.
[11] Witkop and Patrick, *J. Amer. Chem. Soc.*, 1953, **75**, 4474; Brook and Karrer, *Helv. Chim. Acta*, 1957, **40**, 260.
[12] (*a*) Lutz and Hinkley, *J. Amer. Chem. Soc.*, 1950, **72**, 4091; (*b*) Micovic and Mihailovic, "Lithium Aluminium Hydride in Organic Chemistry," Monograph Serbian Acad. Sciences, 1955, Vol. IX, p. 1937.
[13] Djerassi and Thomas, *J. Amer. Chem. Soc.*, 1957, **79**, 3838.
[14] Cf. Braude, Brook, and Linstead, *J.*, 1954, 3569; Agnello and Laubach, *J. Amer. Chem. Soc.*, 1957, **79**, 1257; Campbell and Kidd, *J.*, 1954, 2154.
[15] Cf. Braude, Hanah, and Linstead, *J.*, 1960, 3249; Latif, Fathy, Mishriky, and Atallah, *J. Org. Chem.*, 1960, **25**, 1618.

(3,4-*Dimethoxyphenethylaminomethyl*)*isobutylmalonic Acid*.—Similarly isobutylmalonic acid (176 g.) gave the corresponding *acid* (295 g.), m. p. 148° (decomp.) (Found: C, 60·7; H, 7·7; N, 3·8%).

2-(3,4-*Dimethoxyphenethylaminomethyl*)*hexanoic Acid*.—The n-butylmalonic acid (175 g.) in 60% acetic acid (1800 c.c.) was boiled under reflux for 10 hr. The solvent was removed and the *hexanoic acid* crystallised from ethanol–ether, forming plates (76 g.), m. p. 147—149° (Found: C, 66·1; H, 9·0; N, 4·7. $C_{17}H_{27}NO_4$ requires C, 66·0; H, 8·8; N, 4·5%).

2-(3,4-*Dimethoxyphenethylaminomethyl*)-4-*methylpentanoic Acid*.—Similarly, decarboxylation of the isobutylmalonic acid (175 g.) gave the *pentanoic acid* (76 g.) as prisms (from ethanol–ether), m. p. 162—163° (Found: C, 66·0; H, 8·9%).

1-(3,4-*Dimethoxyphenethyl*)-5-*ethyl*-2-*oxopiperidine*-4-*spiro*-2′-(1′,3′-*dioxolan*) (II).—The ketal was prepared according to the directions of Ban [48] from compound (I; R = Et) (12·6 g.) as a gum (12·2 g.) which crystallised. Recrystallisation from light petroleum (b. p. 40—60°) gave prisms, m. p. 65—68° (Found: C, 65·4; H, 7·8; N, 4·0. Calc. for $C_{19}H_{27}NO_5$: C, 65·3; H, 7·8; N, 4·0%).

3-*Ethyl*-1,2,3,4,6,7-*hexahydro*-9,10-*dimethoxy*-2-*oxobenzo*[a]*quinolizinium Iodide* (III).—The ketal (II; R = Et) (7·9 g.), dry toluene (30 c.c.), and phosphorus oxychloride (20 c.c.) were heated in a boiling-water bath for 3 hr. The solution was taken to dryness under reduced pressure and the residue warmed with 2N-hydrochloric acid (30 c.c.) for 5 min. at 50—60°. The filtered, cooled solution was treated with potassium iodide solution, and the oily iodide was extracted into chloroform. This iodide * crystallised from methanol–ether as yellow prisms (6·86 g.; 73%), m. p.s 171—172·5° (decomp.) (resolidifies at 180°), 240—241° (decomp.) (Found: C, 48·6, 48·35, 48·3; H, 5·4, 5·2, 5·4; N, 3·2, 2·9, 3·35; I, 29·7. $C_{17}H_{22}INO_3,0{\cdot}5H_2O$ requires C, 48·1; H, 5·5; N, 3·3; I, 29·9%), $\nu_{max.}$ 1630s, 1610m, 1560s, and 1530s cm.$^{-1}$.

3-*Ethyl*-3,4,6,7-*tetrahydro*-9,10-*dimethoxy*-2-*oxo*-2H-*benzo*[a]*quinolizine* (IV; R = Et).—(*a*) Cyclisation of the ketal was carried out as described above; after the acid hydrolysis the solution was made alkaline with an excess of 2N-sodium hydroxide, and the precipitated *base* * was extracted with benzene. It crystallised from ethyl acetate as yellow prisms (45%), m. p. 169—171·5° (Found: C, 70·9; H, 7·4; N, 5·0. $C_{17}H_{21}NO_3$ requires C, 71·0; H, 7·4; N, 4·9%). $\nu_{max.}$ 1698w, 1685w, 1670w, 1615s, 1585s, and 1545s cm.$^{-1}$.

The *hydrochloride* * separated from methanol–ether as pale yellow prisms, m. p. 222·5—224° (decomp.) (Found: C, 62·8; H, 6·85; Cl, 11·55. $C_{17}H_{21}NO_3,HCl$ requires C, 63·1; H, 6·85; Cl, 10·95%). The hydriodide,* crystallised similarly, had m. p. 215—217° (decomp.), $\nu_{max.}$ 1640s, 1615m, 1580sh, 1570s, and 1530 cm.$^{-1}$. Comparison of this spectrum with the spectrum of compound (III) also showed many differences in the " finger-print region."

(*b*) Cyclisation of the ketal (6·1 g.) as described above, and subsequent treatment with an excess of 20% aqueous hydrobromic acid and concentration to dryness, gave, after crystallisation, the *hydrobromide* * (3·30 g.), m. p. 225—228°, of base (IV) (Found: C, 55·6; H, 6·1; N, 3·85; Br, 21·0. $C_{17}H_{21}NO_3,HBr$ requires C, 55·4; H, 6·0; N, 3·8; Br, 21·7%), $\nu_{max.}$ 1635m, 1610s, 1565s, and 1515 cm.$^{-1}$.

(*c*) Treatment of the quaternary iodide (III) in methanol with 2N-sodium hydroxide, followed by extraction with benzene and crystallisation of the base from ethyl acetate, gave the base (IV), m. p. and mixed m. p. 168—170°.

(*d*) 3-Ethyl-1,3,4,6,7,11b-hexahydro-9,10-dimethoxy-2-oxo-2*H*-benzo[*a*]quinolizine (0·578g.) in benzene (15 c.c.) was refluxed with chloranil (0·49 g.) for 2·5 hr. The benzene solution was washed 3 times with 2N-sodium hydroxide, then with water, and dried (Na_2SO_4). The product crystallised from ethyl acetate, to give the base (IV) (0·38 g., 65%), m. p. and mixed m. p. 167·5—170·5°; the hydrochloride had m. p. 225—228°, $\lambda_{max.}$ 239, 288, and 360 mμ.

3-*Butyl*-3,4,6,7-*tetrahydro*-9,10-*dimethoxy*-2-*oxo*-2H-*benzo*[a]*quinolizine* (IV; R = Bu).—(*a*) The ketal (II; R = Bu^n) [non-crystalline; 4·37 g.; prepared (cf. refs. 4) in 56% overall yield from 2-(3,4-dimethoxyphenethylaminomethyl)hexanoic acid without characterisation of the intermediates] was heated in toluene (20 c.c.) and phosphorus oxychloride (10 c.c.) at 95° for 3 hr. Isolation of the *base* * as described above and crystallisation from ethyl acetate gave yellow needles (1·5 g., 41%), m. p. 181—183° (Found: C, 72·2; H, 8·0; N, 4·7. $C_{19}H_{25}NO_3$ requires C, 72·35; H, 8·0; N, 4·4%). Comparison with the specimen prepared as in (*b*) below, by mixed m. p. and infrared spectra, showed the two to be identical.

(*b*) 3-Butyl-1,3,4,6,7,11*b*-hexahydro-9,10-dimethoxy-2-oxo-2*H*-benzo[*a*]quinolizine [16] (3·17 g.) and chloranil (2·6 g.) in benzene (100 c.c.) were boiled under reflux for 2·5 hr. The yellow

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crystals, m. p. 181—182·5° (2·14 g.), were filtered off, washed with 2N-sodium hydroxide and water and crystallised from methanol. An *adduct* composed of the tetrahydro-base (IV; R = Bu^n) and the quinol (2 : 1) separated; it had m. p. 183—185° [Found: C, 60·65, 60·4; H, 5·95, 6·1; N, 3·1, 3·2. $(C_{19}H_{25}NO_3)_2,C_6H_2Cl_4O_2$ requires C, 60·1; H, 5·8; N, 3·2%). The *hydrobromide* * of base (IV; R = Bu^n) crystallised from ethanol–ether as yellow prisms, m. p. 217—219° (Found: C, 58·0; H, 6·65; N, 3·5. $C_{19}H_{25}NO_3,HBr$ requires C, 57·6; H, 6·6; N, 3·5%). The base from the hydrobromide separated from ethyl acetate as needles, m. p. 180—182·5° (Found: C, 71·7; H, 7·7; N, 4·7%). The *hydrochloride*, crystallised from methanol–ether and air-dried, had m. p. 187—190° (decomp.) (Found: C, 61·4; H, 7·4; N, 3·9; Cl, 9·7. $C_{19}H_{25}NO_3,HCl,H_2O$ requires C, 61·9; H, 7·4; N, 3·8; Cl, 9·6%).

3,6,7,11*b*-*Tetrahydro*-3-*isobutyl*-9,10-*dimethoxy*-2-*oxo*-2H-*benzo*[a]*quinolizine* (IV; R = Bu^i).—(*a*) The ketal (II; R = Bu^i) [non-crystalline; 5·0 g.; prepared (cf. refs. 4) in 57% overall yield from 2-(3,4-dimethoxyphenethylaminomethyl)-4-methylpentanoic acid] was cyclised as in (*a*) above to the *quinolizine* * (IV) which crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as yellow prisms (1·8 g., 43%), m. p. 156—158° (Found: C, 72·7; H, 7·39; N, 4·4. $C_{19}H_{25}NO_3$ requires C, 72·35; H, 8·0; N, 4·4%), $\nu_{max.}$ 2350w, 1695w, 1640m, 1615s, 1585s, 1550s cm.$^{-1}$. A mixed m. p. with a specimen from (*b*) below, gave no depression.

When the product was processed as described above for the iodide (III), the corresponding quaternary iodide was not isolated. Instead the hydriodide, m. p. 203·5—205° (decomp.) (from methanol–ether), of the base (IV; R = Bu^i) was obtained, identical with that described below (mixed m. p., ultraviolet and infrared spectra). It resisted reduction by potassium borohydride.

(*b*) 1,3,4,6,7,11*b*-Hexahydro-3-isobutyl-9,10-dimethoxy-2-oxo-2*H*-benzo[*a*]quinolizine [18] (3·17 g.) and chloranil (2·6 g.) in benzene (100 c.c.) were boiled under reflux for 2·5 hr., and the solution was washed with 2N-sodium hydroxide and water and dried. The product (1·44 g.) had m. p. 158—160° (from ethyl acetate–light petroleum). The *hydrobromide* * crystallised from ethanol–ether as yellow prisms, m. p. 220—222° (decomp.) (Found: C, 57·85; H, 6·5; N, 3·5. $C_{19}H_{25}NO_3,HBr$ requires C, 57·6; H, 6·6; N, 3·5%). The *hydrochloride*,* air-dried, had m. p. 202—204° (Found: C, 61·45; H, 7·2; N, 3·8; Cl, 10·0. $C_{19}H_{25}NO_3,HCl,H_2O$ requires C, 61·9; H, 7·4; N, 3·8; Cl, 9·6%). The *hydriodide* * had m. p. 210° (decomp.) (Found: C, 51·4; H, 5·9; N, 3·25; I, 28·1. $C_{19}H_{25}NO_3,HI$ requires C, 51·5; H, 5·9; N, 3·2; I, 28·6%), $\nu_{max.}$ 2480w, 1635s, 1600m, 1555—1570s, 1530 cm.$^{-1}$.

3-*Ethyl*-1,3,4,6,7,11*b*-*hexahydro*-9,10-*dimethoxy*-2-*oxo*-2H-*benzo*[a]*quinolizine* (V; R = Et).—(1) The quaternary iodide (III) (2·3 g.) in methanol (100 c.c.) was treated with potassium borohydride (0·2 g.) in two portions at 20°. After 12 hr. the methanol was removed and the residue extracted with a mixture of aqueous sodium carbonate and ether. After drying, the ether was concentrated and the keto-base (V) separated as colourless prisms (1·5 g., 94%); the m. p. and mixed m. p. with an authentic specimen [18] (111—112°) was 111—112·5° (Found: C, 70·6; H, 7·7; N, 4·9. Calc. for $C_{17}H_{23}NO_3$: C, 70·6; H, 8·0; N, 4·8%), $\nu_{max.}$ 1715 cm.$^{-1}$. The hydrochloride * (from ethanol–ether) had m. p. 201·5—202·5° (lit.,[18] m. p. 198—200°) (Found: C, 61·1; H, 7·8; N, 4·1; Cl, 10·7. Calc. for $C_{17}H_{23}O_3N,HCl,0·5H_2O$: C, 61·1; H, 7·55; N, 4·2; Cl, 10·6%). The hydrobromide had m. p. 216·5—217·5° (lit.,[18] m. p. 216—217·5°), $\nu_{max.}$ 3550s, 3450s, 2730s, 1725s, 1630m, 1620m. Attempts to reduce the base, hydrochloride, or hydriodide under the same conditions were ineffective. Similarly, the n-butyl and isobutyl quaternary chloride and iodide and the bases were resistant to reduction by potassium borohydride under various conditions.

(2) The base (IV; R = Et) (1·43 g.) was suspended in dry tetrahydrofuran (25 c.c.), treated portionwise with lithium aluminium hydride (0·3 g.), and refluxed on a water bath for 3 hr. After addition of ethyl acetate, ether, and water, the ethereal extract was dried; it gave a basic residue which was converted into the hydrobromide (0·72 g.), prisms (from methanol–ether), m. p. 220° (decomp.). The base (V) crystallised from light petroleum (b. p. 80—100°), then having m. p. and mixed m. p. 111—113°. An infrared spectrum confirmed that a ketone group was present.

(3) The base (IV; R = Et) (1·43 g.) was suspended in ether (40 c.c.) and added to a solution of lithium (0·16 g.) in liquid ammonia (300 c.c.) at −40°. After 15 minutes' stirring the blue colour had not been discharged, ammonium chloride (1·5 g.) was added, and the yellow solution allowed to evaporate to dryness. Water was added and the basic residue was extracted with

ether and converted into the hydrobromide which separated as nodules (0·55 g.), m. p. 208—209°. The keto-base (V) crystallised from isopropyl ether as needles, m. p. and mixed m. p. [1a] 109—110°.

1,3,4,6,7,11b-*Hexahydro*-3-*isobutyl*-9,10-*dimethoxy*-2-*oxo*-2H-*benzo*[a]*quinolizine* (V; R = Bu^i).—The tetrahydro-base (IV; R = Bu^i) (1·58 g.) was boiled in tetrahydrofuran (25 c.c.) with lithium aluminium hydride (0·34 g.) for 3 hr. The solution was cooled and decomposed with ethyl acetate and water. The product was taken into ether and gave a hydrobromide, prisms (0·9 g.) (from methanol–ether), m. p. 202—204·5° (Found: C, 56·3; H, 7·45. Calc. for $C_{19}H_{27}NO_3,HBr,0{\cdot}5H_2O$: C, 56·1; H, 7·4%), $\lambda_{max.}$ (in 95% EtOH) 232, 284—285 mμ (log ε 3·89, 3·56), $\nu_{max.}$ 2700m, 2580m, 1732s, 1615m, 1525s cm.$^{-1}$. The base from this salt separated from methanol as prisms, m. p. 126—129°. Comparison with an authentic sample [1a] (m. p. 128—130°) by mixed m. p. and infrared absorption showed their identity.

3-*Butyl*-1,3,4,6,7,11b-*Hexahydro*-9,10-*dimethoxy*-2-*oxo*-1H-*benzo*[a]*quinolizine* (V; R = Bu^n).—Similarly, the n-butyl base (IV) (1·0 g.) was reduced with lithium aluminium hydride. The product was isolated as the hydrochloride which crystallised from 2N-hydrochloric acid as prisms (0·2 g.), m. p. and mixed m. p. [1a] 198—199°.

3-*Ethyl*-1,3,4,6,7,11b-*hexahydro*-2-*hydroxy*-9,10-*dimethoxy*-2H-*benzo*[a]*quinolizine* (VII; R = Et).—The keto-base (IV; R = Et) (0·6 g.) in methanol (15 c.c.) was hydrogenated with palladised charcoal (1 g.) at 20°/atm. (uptake of 2 mol. fairly rapid). After filtration, the methanol was removed. The alcohol crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as needles (0·2 g.), m. p. 155—157°, $\nu_{max.}$ 3160s, 1615w cm.$^{-1}$. A mixed melting point with an authentic specimen [1b] (m. p. 156—158°) gave no depression. The hydrobromide had m. p. 231·5—233° (lit.,[1b] m. p. 231—233°).

Catalytic reduction of the ketone (V) with Adams catalyst in methanol gave the same alcohol, m. p. 151—152°, in good yield.

3-*Ethyl*-6,7-*dihydro*-2-*hydroxy*-9,10-*dimethoxybenzo*[a]*quinolizinium iodide* (VI).—The iodide (III) (1·0 g.) was heated at 180° for 10 min.; it frothed and then resolidified. The residue crystallised from methanol, the quaternary *iodide* * (VI) separating as yellow prisms (0·5 g.), m. p. 248° (Found: C, 49·5; H, 4·9; N, 3·4. $C_{17}H_{20}INO_3$ requires C, 49·3; H, 4·9; N, 3·4%), $\nu_{max.}$ 3550m, 1640m, and 1610m cm.$^{-1}$.

Treatment of the iodide in water and methanol with 2N-sodium carbonate gave the dihydrobenzo[*a*]quinolizine base, m. p. 227—230° alone or mixed with an authentic specimen [1a] (m. p. 229—231°). When the hydriodide of the αβ-unsaturated ketone (IV; R = Et) was treated in a similar manner, the salt was recovered unchanged.

(2) 3-Ethyl-1,3,4,6,7,11*b*-hexahydro-2-oxo-9,10-dimethoxy-2*H*-benzo[*a*]quinolizine (V; R = Et) (1·45 g., 1 mol.) was heated in 10% acetic acid (100 c.c.) with mercuric acetate (3·18 g., 2 mol.) at 90—95° for 3 hr., during which mercury separated but no mercurous acetate appeared to be formed. Hydrogen sulphide was passed into the hot solution, charcoal was added, and after filtration the filtrate was treated with an excess of hydrobromic acid. The benzo[*a*]-quinolizinium bromide (1·10 g., 60%) separated as needles, m. p. 257—258°. The filtrate after removal of this salt was examined for the αβ-unsaturated ketone (IV; R = Et); none could be isolated. Use of only 1·59 g. (1 mol.) of mercuric acetate at 60° gave only unchanged starting material.

(3) When the αβ-unsaturated ketone (IV; R = Et) was treated with an excess of mercuric acetate in acetic acid, as described in (2), the quaternary bromide (VI) was isolated as before, having m. p. and mixed m. p. 257—258°.

3-*Ethyl*-3,4,6,7-*tetrahydro*-9,10-*dimethoxybenzo*[a]*quinolizinium Bromide* (VIII).—Mercuric acetate (4 g.) and 3-ethyl-1,3,4,6,7,11*b*-hexahydro-2-hydroxy-9,10-dimethoxy-2*H*-benzo[*a*]-quinolizine (VII; R = Et) (1·45 g.) were heated in 10% acetic acid (75 c.c.) at 95° for 3 hr. The solution became yellow and after 0·5 hr. mercurous acetate and some mercury were precipitated. The product was worked up as in the above experiment and isolated as the *bromide* * (1·62 g., 92%) which separated from methanol–ether as yellow needles, m. p. 265—266° (decomp.) (Found: C, 58·2; H, 5·9; N, 3·9; Br, 22·0. $C_{17}H_{22}BrNO_3$ requires C, 57·95; H, 6·3; N, 4·0; Br, 22·7%). The infrared spectra in Nujol and hexachlorobutadiene showed no NH^+ band in the 2600 cm.$^{-1}$ region.

3-*Ethyl*-3,6,7,11*b*-*tetrahydro*-9,10-*dimethoxy*-4H-*benzo*[a]*quinolizine Hydrobromide* (cf. IX).—Potassium borohydride (0·25 g.) was added to a solution of the above quaternary bromide (VIII) (1·0 g.) in methanol (30 c.c.) at 20°. The yellow-green fluorescence rapidly disappeared

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and after 0·5 hr. 2N-sodium carbonate was added and the base extracted with ether. The *hydrobromide* [8] crystallised from methanol–ether as colourless needles (0·85 g.), m. p. 234—235° (Found: C, 57·5; H, 6·9; N, 3·7. $C_{17}H_{23}NO_2$,HBr requires C, 57·6; H, 6·8; N, 3·95%). $\nu_{max.}$ 2690s, 2600s, 1615m, 1525m cm.$^{-1}$.

3-*Ethyl*-1,3,4,6,7,11*b*-*hexahydro*-9,10-*dimethoxy*-2H-*benzo*[a]*quinolizine Hydrobromide* (cf. X).—The hydrobromide (0·37 g.) of base (IX) was hydrogenated in methanol (30 c.c.) at 20° and 1 atm. in the presence of Adams catalyst (0·05 g.). After an uptake of 26 c.c. ($1H_2$ = 24 c.c) the filtered solution yielded the *hydrobromide* (IX) as colourless prisms (from methanol–ether), m. p. 249—250° (Found: C, 57·1; H, 7·2; N, 3·8. $C_{17}H_{25}NO_2$,HBr requires C, 57·3; H, 7·35; N, 3·9%), $\nu_{max.}$ 2700s, 2640s, 2580s, 1615m, and 1525 cm.$^{-1}$.

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931. *Cyclitols. Part XI.*[1] *The Constitution of Liriodendritol.*

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Liriodendritol (from *Liriodendron tulipifera* L.) is shown to be (1*S*)-1,4-di-*O*-methylmyoinositol.

LIRIODENDRITOL is the only inositol ether known to occur in Nature whose constitution has not yet been determined. Plouvier, who isolated [2] it from *Liriodendron tulipifera* L., proved that it is a dimethyl ether of myoinositol. It is now shown that liriodendritol is (1*S*)-1,4-di-*O*-methylmyoinositol [3] (I). As in all other naturally occurring inositol ethers, the methoxy-groups in liriodendritol are equatorial.

Partial demethylation of liriodendritol, by short heating with hydriodic acid,[4] gave (—)-bornesitol [(1*S*)-1-*O*-methylmyoinositol [5]] (II) in good yield, thereby establishing the position of one methyl group. A second monomethyl ether could not, however, be isolated.

Liriodendritol reacts rapidly with one mol. of periodate, but after this stage further oxidation is slow. The consumption reaches two mol. after several hours, and titration then shows that approximately one mol. of acid has been formed. Some of this acid is present as an ester, titratable only after hydrolysis. The behaviour of liriodendritol on periodate oxidation appeared similar to that of dambonitol [4] and it was at first concluded that the methoxy-groups were *meta* to each other. (Hence the erroneous 1,5-di-*O*-methylmyoinositol structure for liriodendritol in *Adv. Carbohydrate Chem.*, 1959, **14**, 172 and 197.) The consumption of periodate, however, continues over a long period and is not yet complete after 9 days when 4·8 mol. have reacted; there is also a slow increase in the amount of free and " bound " acid formed (see Table).

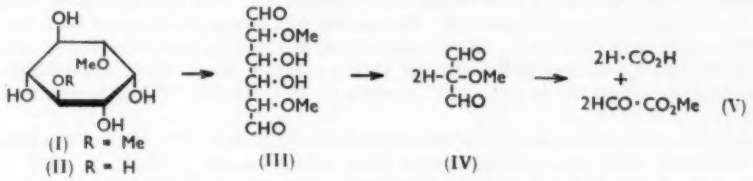
This behaviour is in accord with the annexed sequence, expected [6] for a *para*-di-*O*-methylinositol. The initially formed dialdehyde (III) probably exists mostly in (non-oxidisable) cyclic hemiacetal forms and hence its further oxidation is slow. By analogy with its *O*-benzyl derivative,[7] *O*-methyltartronaldehyde (IV) would be expected to be oxidised to formic acid and methyl glyoxylate; attempts to isolate the dialdehyde (IV) were unsuccessful but its presence was indicated by the decolorisation of iodine in sodium hydrogen carbonate solution, a characteristic reaction of reductones.[8] Methyl glyoxylate

[1] Part X, Angyal and Tate, *J.*, 1961, 4122.
[2] Plouvier, *Compt. rend.*, 1955, **241**, 765.
[3] Nomenclature according to Angyal and Gilham, *J.*, 1957, 3691.
[4] Angyal, Gilham, and Macdonald, *J.*, 1957, 1417.
[5] Bien and Ginsburg, *J.*, 1958, 3189; Anderson and Post, Abs. Papers Amer. Chem. Soc., 1958, **134**, 13D.
[6] Angyal and Klavins, *Austral. J. Chem.*, 1961, in the press.
[7] Schwarz and MacDougall, *J.*, 1956, 3065.
[8] Euler and Eistert, " Reduktone und Reduktonate," Ferdinand Enke, Stuttgart, 1957, p. 7.

Periodate oxidation of liriodendritol (L) and of (±)-1,4-di-*O*-methylmyoinositol (R).

Time	Periodate (mol.)		Free acid (mol.)		Total acid (mol.)		Time	Periodate (mol.)		Free acid (mol.)		Total acid (mol.)	
(hr.)	L	R	L	R	L	R	(hr.)	L	R	L	R	L	R
0·33	1·40	1·40	—	—	—	—	49	3·65	3·59	1·20	1·17	1·87	1·85
7	2·05	1·99	0·46	0·46	0·67	0·62	120	4·36	4·33	1·53	1·55	2·48	2·36
24	2·83	2·80	0·72	0·72	0·88	0·90	168	—	4·54	—	1·63	—	2·77
							216	—	4·81	—	—	—	—

(V) was obtained as its phenylhydrazone; its isolation proves the constitution of liriodendritol because it could not have been formed from an *ortho*- or a *meta*-dimethyl ether.



(I) R = Me
(II) R = H
(III)
(IV)
(V)

The bound acid found by titration is not a formate ester (the " bound formate " often obtained in the periodate oxidations of reducing sugars [9]) but methyl glyoxylate. Part of the titration for free acid is due to *O*-methyltartronaldehyde which, like other substituted malonaldehydes, can be titrated as a monobasic acid to the phenolphthalein end-point.

To confirm the 1,4-dimethyl structure of liriodendritol, the corresponding racemate was synthesised by methylation of 1,2:4,5-di-*O*-cyclohexylidenemyoinositol,[10] followed by hydrolysis of the ketal groups. The resulting dimethyl compound had the same R_F value in several solvent systems, and showed the same behaviour with periodate (Table), as liriodendritol; the tetra-acetates of the two compounds had identical infrared spectra in chloroform solution.

It was pointed out previously [4] that in Nature each inositol methyl ether is accompanied by its parent inositol; dambonitol, a dimethyl ether, is also accompanied by bornesitol, the corresponding monomethyl ether. Liriodendritol is no exception: chromatographic evidence indicates that *L. tulipifera* contains small amounts of myoinositol and 1- and 4-*O*-methylmyoinositol, as well as liriodendritol.

[*Added, September 4th*, 1961.] Liriodendritol itself has been synthesised from (−)-bornesitol. Treatment [11] of the latter with acetone diethyl ketal gave 2,3:5,6-di-*O*-isopropylidenebornesitol [5] (in addition to the 2,3:4,5-derivative) which was converted by methylation and subsequent removal of the isopropylidene groups into a dimethyl ether, identical with natural liriodendritol.

Experimental

Liriodendritol (1·25 g.), m. p. 223°, was isolated from dried autumn leaves of *L. tulipifera* (445 g.) as described by Plouvier.[3] The ethanolic mother liquors were concentrated and examined by paper chromatography in butan-1-ol–pyridine–water (6 : 4 : 3): glucose (R_G 1·0), liriodendritol (0·52), 4-*O*-methylmyoinositol (0·31), 1-*O*-methylmyoinositol (0·19), and myoinositol (0·06) were identified. The amount of the monomethyl ethers was insufficient to allow their separation and the determination of their optical activity.

Partial Demethylation.—Liriodendritol (0·36 g.) was heated on a steam bath with concentrated hydriodic acid (0·72 ml.) for 5 min. The acid was removed in a desiccator over sodium hydroxide, and the residue was dissolved in water and extracted with chloroform to remove the iodine. The concentrated solution was then placed on a cellulose powder column and was eluted with 1 : 4 water–acetone. Fractions 1—13 (127 mg.) contained liriodendritol, and fractions 37—50 mainly myoinositol. Fractions 14—36 were evaporated and the residue

[9] Bobbitt, *Adv. Carbohydrate Chem.*, 1956, **11**, 35.
[10] Angyal, Tate, and Gero, *J.*, 1961, 4116.
[11] Angyal and Hoskinson, unpublished work.

was dissolved in hot ethanol: (−)-bornesitol (61 mg.) crystallised. After two recrystallisations it had m. p. 200°, $[\alpha]_D^{18}$ −25° (*c* 2 in H_2O) (lit.,[2,4] m. p. 203—204°, $[\alpha]_D^{20}$ −32°). The penta-acetate, obtained in 76% yield, had m. p. 140°, $[\alpha]_D^{20}$ −14° (*c* 2 in $CHCl_3$) (lit., m. p. 142°, $[\alpha]_D^{20}$ −11°).

(±)-1,4-*Di*-O-*methylmyoinositol*.—Methyl iodide (65 ml.), and then silver oxide (65 g.), were added in small portions with shaking to a solution of 1,2:4,5-di-*O*-cyclohexylidenemyoinositol (10 g.) in *NN*-dimethylformamide (400 ml.) at <25°. After 3 days' shaking at 28°, more silver oxide (35 g.) was added to the mixture, and shaking was continued for another day. The solids were separated by centrifugation and washed with dimethylformamide and with chloroform. After addition of water (500 ml.) and potassium cyanide (5 g.) the combined supernatant liquid and washings were extracted four times with chloroform. The extracts were shaken with water, dried (Na_2SO_4), and evaporated; the residue was heated on a steam bath for 15 min. with 90% acetic acid (200 ml.). After evaporation, the residue was dissolved in hot ethanol from which (±)-1,4-*di*-O-*methylmyoinositol* (4·5 g., 74%), m. p. 195°, crystallised. Three recrystallisations raised the m. p. to 203° (Found: C, 46·1; H, 7·5. $C_8H_{16}O_6$ requires C, 46·15; H, 7·75%).

Acetylation with acetic anhydride and sulphuric acid gave a 70% yield of the *tetra-acetate*, m. p. 155—156° after two crystallisations from ethanol–water (Found: C, 51·1; H, 6·35. $C_{16}H_{24}O_{10}$ requires C, 51·1; H, 6·4%). The infrared spectrum of this compound, taken on a 5% solution in $CHCl_3$ with a Perkin-Elmer model 12C instrument and a rock-salt prism, was found identical with that of tetra-*O*-acetyl-liriodendritol (m. p. 139°). Absorption bands were found at the following frequencies: 868w, 889w, 905w, 943s, 955m, 980m, 998m, 1034s, 1068s, 1086s, 1107s, 1145s cm.$^{-1}$.

Periodate Oxidations.—Each dimethyl ether (41·6 mg., 0·2 millimole) was dissolved in 0·03M-sodium metaperiodate (50 ml., 1·5 millimoles) and kept in the dark. Aliquot parts (5 ml.) were analysed at intervals. For the determination of periodate, M-sodium carbonate (2 ml.), 10% potassium iodide solution (1 ml.), and 0·025N-sodium arsenite (15 ml.) were added to one part and, after 15 min., the solution was titrated with 0·025N-iodine. For the estimation of free acid, ethylene glycol (20 drops) was added to an aliquot part and, after 1 hr., the solution was titrated with 0·01N-sodium hydroxide (Methyl Red). Excess of 0·01N-sodium hydroxide (2—6 ml.) was then added; after the lapse of 1 hr., the solution was titrated with 0·01N-hydrochloric acid (Methyl Red) to determine the " bound " acid. The results are shown in the Table.

To show the presence of a reductone in the mixture, it was treated with ethylene glycol, followed after 10 min. by sodium hydrogen carbonate: the resulting solution decolorised 0·01N-iodine but no sharp end point was obtained. Reductone was detected after only 20 min. of oxidation.

Isolation of Methyl Glyoxylate Phenylhydrazone.—A solution of 1,4-di-*O*-methylmyoinositol (1 g.) and sodium metaperiodate (7·5 g.) in water (170 ml.) was set aside for a week in the dark. Periodate and iodate were destroyed by sulphur dioxide, and the solution was concentrated *in vacuo* to 100 ml., neutralised with sodium hydrogen carbonate, and filtered. To the filtrate a solution of phenylhydrazine hydrochloride (2 g.) and sodium acetate (3 g.) in water (50 ml.) was added; the resulting precipitate (0·38 g., 22%) gave yellow-brown crystals, having m. p. 136° after two recrystallisations from benzene–light petroleum. They did not depress the m. p. (135°) of methyl glyoxylate phenylhydrazone, prepared by the periodate oxidation of methyl tartrate.

[*Added, September* 4th, 1961.] *Liriodendritol*.—A mixture of (1*S*)-2,3:5,6-di-*O*-isopropylidene-1-*O*-methylmyoinositol[5,11] (17 mg.), *NN*-dimethylformamide (0·3 ml.), methyl iodide (1 ml.), and silver oxide (75 mg.) was shaken at 20° for 15 hr. The solids were separated and washed with dimethylformamide and chloroform. The filtrate was shaken with 5% potassium cyanide solution, and the organic layer was washed with water and evaporated. The residual solid was heated with a few drops of N-hydrochloric acid on the steam bath for 10 min.; the solution was evaporated and the residue dissolved in hot ethanol. On cooling, crystals (9 mg., 70%) were deposited which were identified with liriodendritol by appearance (triangular plates), m. p. 224—225°, and mixed m. p.

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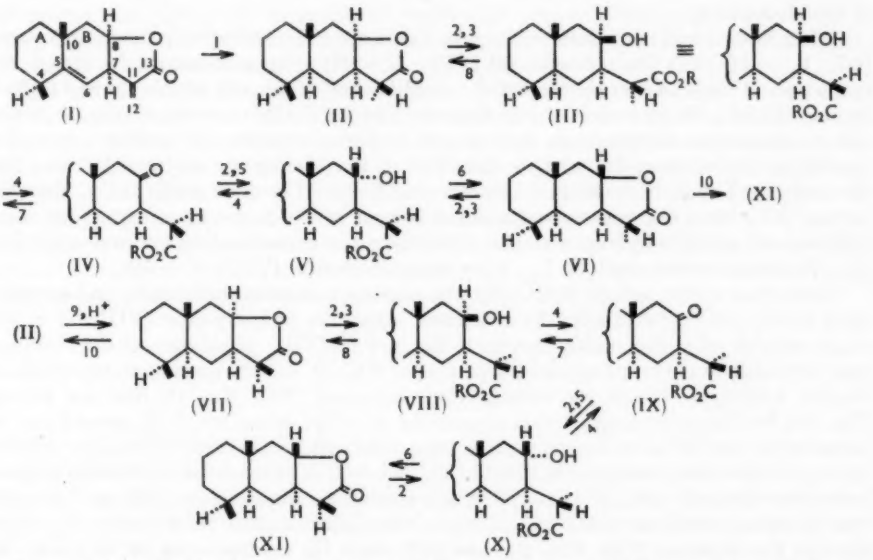
932. *Some Reduction Products of Helenin.*

By Wesley Cocker, L. O. Hopkins, T. B. H. McMurry, and M. A. Nisbet.

Several tetrahydroalantolactones have been inter-related, and their stereochemistry is here discussed.

Helenin consists of a mixture of alantolactone (I), isoalantolactone, and dihydroisoalantolactone, in which alantolactone is predominant. Hydrogenation of helenin over a metal catalyst affords a tetrahydroalantolactone,[1] whose stereo-formula is known to be



Reagents: 1, H_2–Pt. 2, OH^-. 3, CH_2N_2. 4, $Na_2Cr_2O_7$–AcOH. 5, Na–PrⁱOH. 6, p-$C_6H_4Me{\cdot}SO_3H$. 7, KBH_4. 8, Heat. 9, OH^- at 210°. 10, K_2CO_3 in tetralin.

(II).[2,3,4] The course of this hydrogenation is interesting in that hydrogen is added to the 5,6-double bond from the less hindered α-side of the molecule, whilst the other double bond is apparently attacked from the β-side. It is probable, however, that 1,4-addition of hydrogen to the unsaturated lactone system takes place and is followed by isomerisation of the resulting enol to the more stable lactone (II).[5] This lactone has been converted[3,4] into the corresponding *trans*-fused lactone (VI) through the stages (III; R = H) ⟶ (III; R = Me) ⟶ (IV; R = Me) ⟶ (IV; R = H) ⟶ (V; R = H) ⟶ (VI), by employing the reagents shown in the Chart. The lactone (VI) may be reconverted into tetrahydroalantolactone (II) in good yield,[4] by methods also given in the Chart, showing that the series of reactions (II) ⇌ (VI) involves only the configuration at $C_{(8)}$. We have already referred to our successful repetition of the reaction sequence (II)

[1] Ruzicka and van Melsen, *Helv. Chim. Acta*, 1931, **14**, 397; Hansen, *Ber.*, 1931, **64**, 943.
[2] Kovács, Herout, Horák, and Šorm, *Coll. Czech. Chem. Comm.*, 1956, **21**, 225; Benešova, Sýkora, Herout, and Šorm, *Chem. and Ind.*, 1958, 363.
[3] Tsuda, Tanabe, Iwai, and Funakoski, *J. Amer. Chem. Soc.*, 1957, **79**, 5721; cf. Cocker and McMurry, *Tetrahedron*, 1960, **8**, 181.
[4] Cocker, McMurry, and Hopkins, *J.*, 1959, 1998.
[5] Chopra, Cocker, Edward, McMurry, and Stuart, *J.*, 1956, 1828.

to (V; R = H) in an earlier paper;[4] we reported the melting point of the hydroxy-acid (V; R = H) to be 185°, some 10° higher than the previous figure.[3] We have now found, however, that lactonisation of the acid (V; R = H) with toluene-*p*-sulphonic acid in benzene gives a low-melting lactone (VI) (m. p. 38°, $[\alpha]_D$ −70·9°); the compound described by earlier workers[3] had m. p. 75°, $[\alpha]_D$ −29·3°). We have also obtained the low-melting lactone (VI) by treating the hydroxy-acid (V; R = H) with (*a*) boron trifluoride–ether complex and (*b*) toluene-*p*-sulphonic acid in acetic acid, and by treating the methyl ester (V; R = Me) with toluene-*p*-sulphonic acid in benzene. From the hydroxy-acid (V; R = H) in methanolic hydrochloric acid, conditions under which Tsuda *et al.*[3] claim to have obtained the lactone, m. p. 75°, we obtained the methyl ester (V; R = Me) (m. p. 73°; $[\alpha]_D$ +42·3°) which has a similar melting point to this lactone but is quite dissimilar in specific rotation.

When heated with potassium hydroxide, the lactone (II) [effectively the hydroxy-acid (III; R = H)] gives the hydroxy-acid (VIII; R = H) as its potassium salt, though the hydroxy-acid itself has not been isolated. Acidification of this salt affords the 8α,11β(Me)-lactone (VII).[6] We have now shown that this lactone (VII) is converted into its isomer (II) by potassium carbonate in hot tetralin.[7] These experiments confirm our earlier hypotheses[5] concerning the relative stabilities of the 11-epimeric *cis*-fused lactones and the corresponding hydroxy-acids. The lactone (II) should be more stable at $C_{(11)}$ than the lactone (VII) since the former is a *cis*-fused lactone in which the 11-methyl group is *cis* with respect to the 7-hydrogen atom. Conversely the corresponding hydroxy-acid (III; R = H) should be less stable at $C_{(11)}$ than the hydroxy-acid (VIII; R = H).

Hydrolysis of the lactone (VII) with 4% aqueous potassium hydroxide, and esterification of the resulting acid with diazomethane, afford the hydroxy-ester (VIII; R = Me) as an unstable oil which readily reverts to the lactone (VII). Oxidation of the hydroxy-ester with chromium trioxide gives the keto-ester (IX; R = Me), again as an oil, which on alkaline hydrolysis affords the corresponding keto-acid (IX; R = H) (but see below). This acid has the same configuration at position 11 (β-Me) as lactone (VII), since it can be reconverted into the latter in good yield by treatment with borohydride followed by acidification. On the other hand, the keto-acid (IX; R = H) is reduced with sodium in propan-2-ol to the hydroxy-acid (X; R = H) which affords the *trans*-lactone (XI) on treatment with toluene-*p*-sulphonic acid. No configurational change other than that at $C_{(8)}$ takes place in the sequence (IX; R = H) ⟶ (XI) since the reactions can be reversed. In accordance with our previous experience,[5] the lactone (XI) should have greater stability at $C_{(11)}$ than its epimer (VI), since these are *trans*-lactones in which the former has the 11-methyl group *trans* to the 7-hydrogen atom. We have confirmed our deductions by the conversion of the lactone (VI) into its isomer (XI) by potassium carbonate in hot tetralin.[7] We have thus related the four lactones (II), (VI), (VII), and (XI) stereochemically.

Klyne's lactone rule[8] confirms the stereochemistry at position 8 in the lactones (VI) and (XI) as shown in the Table. The hydroxy-acids (III and VIII; R = H) are too

Hydroxy-acid	$[M]_D$	Lactone	$[M]_D$	$\Delta[M_D]$
(V; R = H)	+116·8°	(VI)	−167·3°	−284·1°
(X; R = H)	+63·5	(XI)	−41·1	−104·6
(III; R = H) *	+33·1	(II)	+36·5	+3·4
(VIII; R = H) *	+56·3	(VII)	+68·4	+12·1

* $[M]_D$ measured as sodium salts in aqueous-methanolic solution.

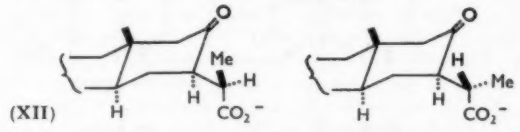
unstable to allow measurement of their molecular rotations. The small shifts in molecular rotations in passing from their sodium salts to the corresponding lactones are in the correct

[6] Asselineau, Bory, and Lederer, *Bull. Soc. chim. France*, 1955, 1524.
[7] Cocker, Cross, and Lipman, *J.*, 1949, 959.
[8] Klyne, *Chem. and Ind.*, 1954, 1198.

direction for our stereo-formulæ (II) and (VII). However, molecular rotations of sodium salts in solution are sometimes anomalous,[9] and too much reliance cannot be placed upon conclusions drawn in this way.

Whilst the *cis*-lactone (II) is readily converted [6] into the *cis*-lactone (VII) by heating it with potassium hydroxide at 210° or with sodium methoxide (reactions which involve respectively the anions of the corresponding acids, and the esters), neither of the *trans*-hydroxy-acids or esters (V; R = H, Me) and (X; R = H, Me) is similarly affected (cf. refs. 4, 5). These conversions need further investigation.

Hydrolysis of the keto-ester (IX; R = Me) with alkali never gave a good yield of its crystalline acid (IX; R = H). We thought that this might be due to equilibration at position 11 with formation of some of the oily keto-acid (IV; R = H). Since the potassium salts of the keto-acids are stable to alkali under the conditions of hydrolysis of the esters, equilibration would have to take place before the ester hydrolysis. Some support for this suggestion was obtained when the esters (IV; R = Me) and (IX; R = Me) were treated with 3% sodium methoxide in methanol. The oily products from the two esters had the same specific rotation and roughly corresponded to a 2 : 1 mixture of the isomers (IV; R = Me) and (IX; R = Me) respectively, though the change in rotation was small. Reduction of each product with borohydride gave a mixture from which lactone (II) was isolated. The other lactone (VII) could not, however, be isolated. The behaviour of the keto-esters may be explained on the basis of interaction between keto- and ester groups, as suggested by Mazur and Sondheimer.[10] This interaction would bring the two carbonyl groups into close proximity, and the 11-epimers (IV and IX; R = Me) would have the relative order of stability of the *cis*-fused lactones (II) and (VII).



If either of the keto-acids (IV; R = H) and (IX; R = H) is heated with alkali at 220°, acidification then gives a mixture from which only one acid (IX; R = H) is obtained. The carboxylate anions of acids (IV and IX; R = H) must exist as (XII) and (XIII) and the latter is the more stable. In these structures we take no account of the enolates which may be produced. Enolisation of the 8-keto-group would enhance the repulsion of the carboxylate ion.

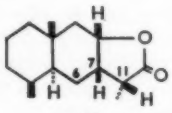
Ukita and Nakasawa [11] recently reported the preparation of a keto-acid, m. p. 153—154°, $[\alpha]_D$ +0·8°, from the lactone (II) under the conditions described for the sequence (II) ⟶ (III) ⟶ (IV; R = H). As mentioned above, we have always obtained the keto-acid as an oil, and Tsuda *et al.*[3] also obtained it as an oil, which we believe is correctly represented by the stereo-formula (IV; R = H). It appears to us that the acid described by Ukita and Nakasawa [11] is the isomer (IX; R = H) which we obtained crystalline, with m. p. 150°, $[\alpha]_D$ −11·7°, and that equilibration of the esters (IV and IX; R = Me) took place under the conditions of ester-hydrolysis employed by Ukita and Nakasawa. It is clear, therefore, that care must be taken in interpreting the results of such reactions which involve alkaline conditions, unless the reactions can be reversed to give starting materials in good yields.

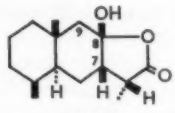
We must now comment on the lactone, m. p. 110—112°, $[\alpha]_D$ −29·2°, which is obtained [3,4] in low yield along with the hydroxy-acid (V; R = H) when the keto-acid (IV; R = H) is reduced with sodium in propan-2-ol. In our earlier paper [4] we assigned to this lactone the configuration shown as (XI) on the ground that three of the four possible

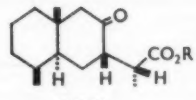
[9] Sýkora and Románuk, *Coll. Czech. Chem. Comm.*, 1957, **22**, 1909.
[10] Mazur and Sondheimer, *Experientia*, 1960, **16**, 181.
[11] Ukita and Nakasawa, *J. Amer. Chem. Soc.*, 1960, **82**, 2224.

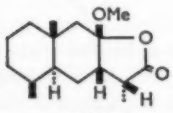
lactones (II, VI, VII) differing in configuration only at positions 8 and 11 were already known. Since we have now prepared and stereochemically related all four lactones, our earlier conclusion was invalid. We have now shown that the lactone has structure (XIV) with the " unnatural " configuration at position 7.

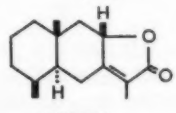
We arrive at our assignment of structure on the following grounds. The lactone, m. p. 112°, can be obtained by borohydride reduction of the acidic hydroxy-lactone, now shown to be (XV), which was obtained [3] in low yield, together with the oily keto-acid (IV; R = H), by alkaline hydrolysis of the keto-ester (IV; R = Me). The mild conditions of the reduction imply a close relationship between (XIV) and (XV). The 7β(H)-hydroxy-lactone (XV) shows maxima at 3350 (OH) and 1740 cm.$^{-1}$ (lactone), and on hydrolysis with sodium hydroxide in methanol affords the 7α(H)-keto-acid (IV), characterised by reduction with borohydride to tetrahydroalantolactone (II) and with sodium in propan-2-ol to the hydroxy-acid (V). The hydrolysis of hydroxy-lactone (XV) to acid (IV) shows that the former is either the 7α(H)-hydroxy-lactone corresponding to (IV) or the 7β(H)-isomer (XV) which is converted into (IV) *via* the 7β(H)-keto-acid (XVI; R = H) which has an axial three-carbon side chain. Borohydride reduction of the hydroxy-lactone (XV) gives a lactone differing from (II) and (VI), which indicates the structure (XV) assigned to the hydroxy-lactone. The hydroxy-lactone (XV) is probably derived from the corresponding keto-acid (XVI; R = H) which we can assume to be present in small quantities in equilibrium with the much more stable 7α(H)-keto-acid (IV; R = H) during alkaline hydrolysis of the ester of the latter.

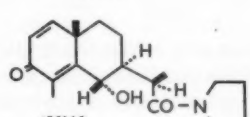

(XIV)


(XV)


(XVI)


(XVII)


(XVIII)


(XIX)

Reaction of diazomethane with the lactone (XV) affords a product which crystallises well but shows three infrared maxima, at 1755 (lactone), 1740 (CO_2Me), and 1710 cm.$^{-1}$ (ketone), and an ultraviolet peak at 2900 Å (log ε 1·49) compared with 2810 Å (log ε 1·94) for the ester (IX; R = Me). The peak at 1755 cm.$^{-1}$ could be attributed to the methoxy-lactone (XVII) though there is no other evidence of its presence.

We have confirmed the finding that the hydroxy-lactone (XV) with either phosphorus oxychloride in pyridine or toluene-*p*-sulphonic acid in benzene affords [3] the unsaturated lactone (XVIII). This product shows maximum absorption at 2200 Å (log ε 4·05). Matsumura, Iwai, and Ohki [12] record $\lambda_{max.}$ 2250 Å (log ε 3·93). The dehydration might be expected to afford an 8,9-double bond, but models of this unsaturated compound show it to be highly strained, and dehydration must proceed in the other direction to give the 7,8-double bond (a *cis*-elimination), which rearranges in the acid conditions to the 7,11-position.

The structure (XV) for the hydroxy-lactone leads to the structure (XIV) for the lactone, m. p. 112°. We assign to it the 8β(H)-configuration for two reasons. (*a*) The alcoholic hydroxyl group participating in the lactone formation is formed by reduction of the 8-keto-group with sodium in propan-2-ol, and hence must be equatorial. (*b*) The lactone must

[12] Matsumura, Iwai, and Ohki, *J. Pharm. Soc. Japan*, 1954, **74**, 1029.

be *cis*-fused since the corresponding *trans*-fused lactone requires that ring B should exist in a boat form, which would be difficult to prepare from the hydroxy-acid [13] and would be readily hydrolysed to the latter. In fact, the lactone (XIV) is difficult to hydrolyse, and hydrolysis and careful acidification of the lactone affords only starting material.

The 11β(H)-configuration assigned to lactone (XIV) is the less stable of the two possibilities since there is considerable interference between the 6-methylene and the 11α-methyl group. We were unable, however, to epimerise this centre by the use of potassium carbonate in boiling tetralin, and potassium hydroxide at 210° does not affect it. Epimerisation with potassium carbonate in tetralin is almost certainly a surface reaction and the less planar molecule of (XIV) produced by the large axial 7-substituent may prevent the reaction from occurring. A lactone with the $C_{(11)}$-configuration of lactone (XIV) would not be expected to epimerise with potassium hydroxide.[4,5] Our assignment of configuration at position 11 is therefore based on the production of keto-acid (IV) when the lactone (XV) is hydrolysed. This keto-acid is the less stable (see above) of the two 11-epimers and therefore cannot have undergone epimerisation at position 11.

The lactone (XIV) gives a sparingly soluble sodium salt, attempted oxidation of which with *N*-bromosuccinimide in phosphate buffer,[14] or with chromium trioxide in pyridine, yielded only the starting material. The lactone was unaffected by pyrrolidine in benzene, under which conditions santonin yielded the hydroxy-amide (XIX).

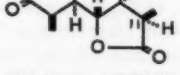
Experimental

Infrared spectra were measured with a Perkin-Elmer Infracord spectrophotometer for Nujol suspensions unless otherwise stated. $[\alpha]_D$ refers to $CHCl_3$ solutions unless otherwise stated.

Methyl 8α-*Hydroxy*-4,5,11α(H)-*eudesman*-13-*oate* * (V; R = Me).—(*a*) The hydroxy-acid [3,4] (V; R = H) (100 mg.) in methanol (5 c.c.) was set aside with an excess of ethereal diazomethane. The product was the *hydroxy-ester* (V; R = Me) (80 mg.) which crystallised from aqueous methanol as plates, m. p. 73—74°, $[\alpha]_D^{16}$ +42·5° (*c* 0·20), $\nu_{max.}$ 3450 (OH), 1725 cm.$^{-1}$ (ester) (Found: C, 71·2; H, 10·4. $C_{16}H_{28}O_3$ requires C, 71·6; H, 10·5%). (*b*) The hydroxy-acid (270 mg.) was refluxed with methanol (10 c.c.) and 10% hydrochloric acid (5 c.c.) for 5 min. The product, crystallised from aqueous methanol, was the hydroxy-ester (200 mg.), m. p. and mixed m. p. 73°.

4,5α(H),8,11β(H)-*Eudesman*-8,13-*olide* (VI).—(*a*) The hydroxy-acid (V; R = H) (40 mg.) was refluxed in benzene (5 c.c.) with toluene-*p*-sulphonic acid (9 mg.) for 30 min. The product was chromatographed on " Woelm " brand acid alumina, and eluted with mixtures of light petroleum (b. p. 40—60°) and benzene. The *lactone* (VI) (31 mg.) obtained was crystallised from 95% methanol, forming plates, m. p. 38°, $[\alpha]_D^{14·5}$ −70·9° (*c* 0·43), $\nu_{max.}$ 1795 (lactone) 1285 cm.$^{-1}$ (C–O) (Found: C, 75·6; H, 10·4. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·2%). (*b*) Similar treatment of the hydroxy-ester (V; R = Me) (12 mg.) afforded the lactone (VI) (9 mg.), m. p. and mixed m. p. 34°. (*c*) The hydroxy-acid (V; R = H) (500 mg.) was set aside for 1 hr. with boron trifluoride–ether complex (7 c.c.). The product, chromatographed as described above, gave the lactone (200 mg.), m. p. and mixed m. p. 34°. (*d*) The hydroxy-acid (V; R = H) (150 mg.) was refluxed in acetic acid (10 c.c.) with toluene-*p*-sulphonic acid

* In the present paper we preserve the nomenclature of our previous paper.[4] This means that the configuration of the 11-hydrogen atom in the acids and esters is related to the 11(H) of the angular lactones, *e.g.*:



[13] Johnson, Bauer, Margrave, Frisch, Dredger, and Hubbard, *J. Amer. Chem. Soc.*, 1961, **83**, 606.
[14] Tahara, *J. Org. Chem.*, 1956, **21**, 442.

(100 mg.) for 30 min., then cooled and poured into water (100 c.c.). The product isolated from ethereal solution was the lactone (VI) (100 mg.), m. p. and mixed m. p. 36°.

Hydrolysis of 4,5α(H),8,11β(H)-*Eudesman*-8,13-*olide* (VI).—The lactone (50 mg.) in methanol (5 c.c.) was refluxed for 2 hr. with 1% methanolic sodium hydroxide (10 c.c.). The mixture was then cooled, poured into water, and neutralised with dilute hydrochloric acid. Methanol was removed under reduced pressure, and the residue was extracted with ether (2 × 10 c.c.). Removal of solvent from the dried extract gave the hydroxy-acid (V; R = H) (40 mg.) which crystallised as plates, m. p. and mixed m. p. 183°.

Epimerisation of 4,5,8,11α(H)-*Eudesman*-8,13-*olide* [6] (VII) *to* 4,5,8α(H),11β(H)-*Eudesman*-8,13-*olide* (II).—The lactone (200 mg.) (Found: C, 76·2; H, 10·45. Calc. for $C_{15}H_{24}O_2$: C, 76·2; H, 10·2%) was refluxed with freshly ignited potassium carbonate (200 mg.) in anhydrous tetralin (10 c.c.) for 4 hr. After filtration, the solvent was removed under reduced pressure, leaving an oil which was chromatographed on "Woelm" brand acid alumina with benzene–light petroleum, giving a solid product. Crystallisation from methanol gave tetrahydroalantolactone (II) (100 mg.), m. p. and mixed m. p. 144—145°.

8-*Oxo*-4,5α(H),11β(H)-*eudesman*-13-*oic Acid* (IX; R = H).—4,5,8,11α(H)-Eudesman-8,13-olide [6] (VII) (2·4 g.) was refluxed with potassium hydroxide (2·2 g.) in water (55 c.c.) until the mixture was homogeneous. The solution was cooled to −5°, ether (100 c.c.) was added, and the mixture was stirred vigorously and carefully neutralised with dilute acetic acid. The ether layer was separated, an excess of ethereal diazomethane was immediately added, and the solution was set aside at −5° for 1 hr. and at 20° for 1 hr. Removal of the solvent afforded the hydroxy-ester (VIII; R = Me) (2·2 g.) as an oil, $[\alpha]_D^{18}$ −4·7° (*c* 0·81), $\nu_{max.}$ 3450 (OH), 1740 cm.$^{-1}$ (CO_2Me). The hydroxy-ester (2·0 g.) in acetic acid (35 c.c.) was added to sodium dichromate (1·0 g.) in acetic acid (35 c.c.), and the mixture was set aside for 1 hr. The excess of dichromate was then reduced with ethanol, and the solution was concentrated under reduced pressure to 30 c.c., poured into water, and extracted with ether (3 × 25 c.c.). The extract was washed with 5% sodium hydrogen carbonate solution and with water. Removal of the solvent afforded the keto-ester (IX; R = Me) as an oil (1·8 g.), $\nu_{max.}$ 1748 (CO_2Me), shoulders at 1786 (lactone?) and 1721 cm.$^{-1}$ (ketone). This product was refluxed for 1·5 hr. with potassium hydroxide (1·0 g.), methanol (15 c.c.) and water (5 c.c.), then the whole was poured into water and extracted with ether (2 × 20 c.c.). The alkaline solution was acidified and extracted with ether (2 × 20 c.c.). The combined ethereal extracts were washed with 10% sodium hydrogen carbonate which was acidified and extracted with ether (3 × 25 c.c.). These combined extracts were washed with water, dried, and evaporated, giving 8-*oxo*-4,5(H),11β(H)-*eudesman*-13-*oic acid* (IX; R = H) (1·2 g.) which crystallised from aqueous ethanol as needles, m. p. 152°, $[\alpha]_D^{19}$ −11·7° (*c* 0·33 in MeOH), $\nu_{max.}$ 1720 cm.$^{-1}$ (C=O and CO_2H) (Found: C, 71·3; H, 9·5. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·6%).

Reduction of 8-*Oxo*-4,5α(H),11β(H)-*eudesman*-13-*oic Acid* (IX; R = H) *with Potassium Borohydride*.—The keto-acid (39 mg.) in methanol (3 c.c.) containing sodium hydrogen carbonate (39 mg.) was treated with a solution of potassium borohydride (50 mg.) in water (1 c.c.), and the mixture was set aside overnight. It was then acidified and diluted with water (10 c.c.), and the deposited solid was crystallised from aqueous ethanol, giving 4,5,8,11α(H)-eudesman-8,13-olide (VII) (29 mg.) as needles, m. p. and mixed m. p. 69—70°.

8α-*Hydroxy*-4,5α(H),11β(H)-*eudesman*-13-*oic Acid* (X; R = H).—Sodium (10 g.) was added slowly to a boiling solution of 8-oxo-4,5α(H),11β-eudesman-13-oic acid (IX; R = H) (800 mg.) in propan-2-ol (100 c.c.), and the mixture was refluxed for a further 3 hr. Further propan-2-ol (30 c.c.) was added to dissolve the remaining sodium, and the mixture was refluxed for 0·5 hr., cooled to 0°, and neutralised with acetic acid. The volume of the mixture was reduced to 30 c.c. under reduced pressure, and the residue was diluted with water (150 c.c.), and extracted with ether (3 × 20 c.c.). The combined extracts were washed with 5% sodium hydrogen carbonate solution, and the washings were acidified. The deposited solid crystallised from aqueous methanol, giving 8α-*hydroxy*-4,5α(H),11β(H)-*eudesman*-13-*oic acid* (X; R = H) as needles (300 mg.), m. p. 162—163°, $[\alpha]_D^{16}$ +25° (*c* 0·27 in MeOH), $\nu_{max.}$ 3550 (OH), 1685 cm.$^{-1}$ (CO_2H) (Found: C, 70·9; H, 10·15. $C_{15}H_{26}O_3$ requires C, 70·8; H, 10·3%). The neutral fraction remaining in the ether solution after it had been washed with sodium hydrogen carbonate afforded a solid which on purification on "Woelm" brand acid alumina (benzene solution; benzene–light petroleum as eluants) gave the lactone (XIV) (70 mg.), m. p. 110°, $[\alpha]_D^{14}$ −29·4° (*c* 0·47), $\nu_{max.}$ 1795 (lactone), 1280 (C–O), and 995 cm.$^{-1}$ (Found: C, 76·2; H,

10·2. Calc. for $C_{15}H_{24}O_2$: C, 76·2; H, 10·2%). This lactone gave no depression of m. p. with the lactone [3,4] obtained along with the hydroxy-acid (V; R = H) when the keto-acid (IV; R = H) was reduced with sodium in propan-2-ol.

4,5,11α(H),8β(H)-*Eudesman*-8,13-*olide* (XI).—The hydroxy-acid (X; R = H) (500 mg.) was refluxed for 30 min. with toluene-*p*-sulphonic acid (100 mg.) and acetic acid (7 c.c.), and the mixture was cooled and poured into water. It was extracted with ether (2 × 10 c.c.), and the combined extracts were washed with 5% sodium hydrogen carbonate solution and with water. The solvent was removed, giving the *lactone* (XI) (400 mg.) which crystallised from methanol as needles, m. p. 92·5° (depressed to 82° by admixture with previous lactone), $[\alpha]_D^{19}$ −17·4° (*c* 0·6), $\nu_{max.}$ 1798 (lactone), 1280 cm.$^{-1}$ (C–O) (Found: C, 76·8; H, 10·25. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·2%).

Hydrolysis of 4,5,11α(H),8β(H)-*Eudesman*-8,13-*olide* (XI).—The lactone (XI) (20 mg.) in methanol (5 c.c.) was refluxed for 2 hr. with 1% methanolic sodium hydroxide (10 c.c.) and then poured into water. The mixture was acidified and then extracted with ether (2 × 10 c.c.) from which 8α-hydroxy-4,5α(H),11β(H)-eudesman-13-oic acid (X; R = H) (15 mg.) was obtained as plates (from aqueous methanol), m. p. and mixed m. p. 161—162°.

Methyl 8α-*Hydroxy*-4,5α(H),11β(H)-*eudesman*-13-*oate* (X; R = Me).—A solution of the hydroxy-acid (X; R = H) (100 mg.) in methanol (5 c.c.) was treated with an excess of diazomethane in ether, and the mixture was set aside for 1 hr. The product was the required *ester* (X; R = Me) (80 mg.) which crystallised from aqueous methanol as needles, m. p. 110°, $[\alpha]_D^{18}$ +50° (*c* 0·05), $\nu_{max.}$ 3250 (OH), 1740 cm.$^{-1}$ (ester) (Found: C, 71·6; H, 10·5. $C_{16}H_{28}O_3$ requires C, 71·6; H, 10·5%).

Reconversion of Methyl 8α-*Hydroxy*-4,5α(H),11β(H)-*eudesman*-13-*oate* (X; R = Me) *into* 4,5,8,11α(H)-*Eudesman*-8,13-*olide* (VII).—The hydroxy-ester (X; R = Me) (100 mg.) was added to sodium dichromate (80 mg.) in acetic acid (8 c.c.) and set aside for 1 hr. The excess of dichromate was decomposed with ethanol, and the solution was concentrated under reduced pressure to 1 c.c. Water was added, the mixture was extracted with ether, and the ethereal extract was washed with 5% sodium hydrogen carbonate and then with water. The solvent was removed, giving the oily keto-ester (IX; R = Me). This was set aside overnight with potassium borohydride (80 mg.) in water (0·5 c.c.) and methanol (5 c.c.). The resulting solution was then filtered and acidified, giving the lactone (VII) (50 mg.) which, when crystallised from aqueous methanol, had m. p. and mixed m. p. 71°.

Epimerisation of 4,5α(H),8,11β(H)-*Eudesman*-8,13-*olide* (VI) *to* 4,5,11α(H),8β(H)-*Eudesman*-8,13-*olide* (XI).—The lactone (VI) (100 mg.) was refluxed for 5 hr. in anhydrous tetralin (10 c.c.) with freshly ignited potassium carbonate (100 mg.). The mixture was filtered, and the tetralin was removed under reduced pressure, giving an oily residue which was chromatographed on "Woelm" brand acid alumina with light petroleum (b. p. 60—80°) and benzene. The solid obtained was crystallised from aqueous methanol, giving 4,5,11α(H),8β(H)-eudesman-8,13-olide (XI) (50 mg.) as needles, m. p. and mixed m. p. 89—91°, $[\alpha]_D^{18}$ −21·5° (*c* 0·20) (Found: C, 75·8; H, 10·1%).

Equilibration of the Keto-esters (IV; R = Me) *and* (IX; R = Me).—(*a*) Methyl 8-oxo-4,5,11α(H)-eudesman-13-oate (IV; R = Me) (60 mg.), $[\alpha]_D^{19}$ −19·6° (*c* 0·20), and 3% methanolic sodium methoxide (3 c.c.) were refluxed for 2 hr. The solution was neutralised with acetic acid, poured into water, and extracted with ether. The extract was washed with water, dried, and treated with diazomethane. Removal of the solvent afforded an oil (54 mg.), $[\alpha]_D^{19}$ −23·2° (*c* 0·537). Reduction of the oil (50 mg.) in methanol (3 c.c.) with potassium borohydride (10 mg.) in water (0·5 c.c.) afforded, after acidification, the lactone (II) (29 mg.) as needles, m. p. 130—134°.

(*b*) Similar treatment of the oily methyl 8-oxo-4,5α(H),11β(H)-eudesman-13-oate (IX; R = Me) (900 mg.), $[\alpha]_D^{19}$ −24·7° (*c* 0·41), with 3% sodium methoxide (6 c.c.) afforded an oil (840 mg.), $[\alpha]_D^{18}$ −22·8° (*c* 0·44). Reduction with potassium borohydride and acidification afforded the lactone (II) (400 mg.), m. p. 135—138°.

Equilibration of the Keto-acids (IV; R = H) *and* (IX; R = H).—(*a*) A mixture of 8-oxo-4,5,11α(H)-eudesman-13-oic acid (IV; R = H) (290 mg.), $[\alpha]_D^{16}$ +12·4° (*c* 0·25 in MeOH), potassium hydroxide (400 mg.), and water (0·5 c.c.) was heated to 220° during 25 min. The mixture of acids (220 mg.) isolated on acidification had a similar spectrum to that of (IV; R = H) and (IX; R = H) and had $[\alpha]_D^{19}$ −7·2° (*c* 0·37 in MeOH). Crystallisation from light petroleum (b. p. 60—80°) gave the keto-acid (IX; R = H) (80 mg.), m. p. and mixed m. p.

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150°. (*b*) Similar treatment of 8-oxo-4,5α(H),11β(H)-eudesman-13-oic acid (IX; R = H) (50 mg.), $[\alpha]_D^{19}$ −11·7° (*c* 0·33 in MeOH), afforded a mixture of acids (40 mg.), $[\alpha]_D^{19}$ −8·0° (*c* 0·19 in MeOH). Crystallisation from light petroleum (b. p. 60—80°) afforded the keto-acid (IX; R = H) (22 mg.), m. p. and mixed m. p. 150°.

8β-*Hydroxy*-4,5α(H),7,11β(H)-*eudesman*-8,13-*olide* (XV).—The product (7 g.) from the hydrolysis of the keto-ester (IV; R = Me) was dissolved in ligroin (200 c.c.) and set aside overnight at 0°. The *lactone* (XV) (350 mg.) separated as cubes, m. p. 147—148°, $[\alpha]_D^{18}$ +9·3° (*c* 0·29) (Tsuda *et al.*[3] record m. p. 141—143°, $[\alpha]_D$ +10·5°) (Found: C, 71·5; H, 9·4. Calc. for $C_{15}H_{24}O_3$: C, 71·4; H, 9·6%).

Treatment of the Hydroxy-lactone (XV) *with Alkali.*—The lactone (360 mg.) was refluxed for 2 hr. with sodium hydroxide (100 mg.) in methanol (4·5 c.c.) and water (0·5 c.c.). The acidic product was an oil (0·02 g.), $\nu_{max.}$ 1685 cm.$^{-1}$, which was set aside overnight with potassium borohydride (20 mg.) in methanol (2 c.c.) and water (0·2 c.c.). The mixture was then acidified, water was added, and the solid product (113 mg.) was collected. Crystallisation from ethanol gave 4,5,8α(H),11β(H)-eudesman-8,13-olide (II), m. p. and mixed m. p. 142°, $[\alpha]_D^{19}$ +8·8° (*c* 0·1).

Reduction of the Hydroxy-lactone (XV) *with Sodium in Propan-2-ol.*—A boiling solution of the lactone (50 mg.) in propan-2-ol (20 c.c.) was slowly treated with sodium (2·5 g.), and the solution was refluxed for a further 3 hr. It was cooled to 0°, neutralised with acetic acid, then concentrated under reduced pressure to 15 c.c., poured into water, and extracted with ether. The ethereal solution was extracted with 3% sodium hydrogen carbonate solution, and the extract was acidified. The solid product was collected and crystallised from aqueous methanol as plates (23 mg.), m. p. 181° alone or mixed with 8α-hydroxy-4,5,11α(H)-eudesman-13-oic acid (V).

Reduction of the Hydroxy-lactone (XV) *with Potassium Borohydride.*—The lactone (30 mg.) in methanol (5 c.c.) was set aside for 26 hr. with potassium borohydride (100 mg.) in water (0·5 c.c.). The mixture was acidified and diluted with water, giving a solid which crystallised from aqueous ethanol as needles (20 mg.), m. p. and mixed m. p. with lactone (XIV) [3,4] 110°, $[\alpha]_D^{17}$ −30·5° (*c* 0·17), $\nu_{max.}$ 1780 cm.$^{-1}$.

Reaction of the Hydroxy-lactone (XV) *with Diazomethane.*—The lactone (80 mg.) in ether (10 c.c.) was treated at 0° with an excess of ethereal diazomethane. After 12 hr. the solvent was removed, giving *methyl* 8-*oxo*-4,5α(H),7,11β(H)-*eudesman*-13-*oate* (XVI; R = Me) which crystallised from aqueous ethanol as needles, m. p. 80—81°, $[\alpha]_D^{18}$ −74·2° (*c* 0·33) (Found: C, 71·7; H, 9·7. $C_{16}H_{26}O_3$ requires C, 72·1; H, 9·8%).

Attempted Epimerisation of the Lactone (XIV).—(*a*) The lactone (100 mg.) was refluxed for 5·5 hr. with freshly ignited potassium carbonate (500 mg.) in tetralin (2 c.c.). The mixture was filtered and the solvent removed under reduced pressure, giving starting material (90 mg.), m. p. and mixed m. p. 112°. (*b*) The lactone (100 mg.) was fused with potassium hydroxide (200 mg.) at 210° for 20 min. The melt was dissolved in water and acidified, giving starting material (80 mg.), m. p. and mixed m. p. 112°.

1-[6α-*Hydroxy*-3-*oxo*-11α(H)-*eudesma*-1,4-*dien*-13-*oyl*]*pyrrolidine* (*Santoninpyrrolidinamide*) (XIX).—Santonin (1 g.) was refluxed in benzene (20 c.c.) with pyrrolidine (1 c.c.) for 4 hr. The solution was washed with dilute hydrochloric acid, then with water, and dried. The benzene was removed, giving the *amide* (800 mg.) as plates (from ethyl acetate–light petroleum), m. p. 159—160°, $[\alpha]_D^{16}$ −45·6° (*c* 1·47), $\nu_{max.}$ (in $CHCl_3$) 3490b,s (OH), 1667 (ketone), 1630 cm.$^{-1}$ (amide and conjugated C=C) (Found: C, 72·3; H, 8·5. $C_{19}H_{27}NO_2$ requires C, 71·9; H, 8·6%).

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933. *Dipole Moment Studies on Polyethylene and Polypropylene Glycols of Low Molecular Weight.*

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Dipole-moment measurements, on the pure solute and on benzene solutions, of polypropylene glycols are reported, as are measurements on some polyethylene glycols. These are compared with theoretical dipole moments calculated by using the equations of Uchida *et al.* and Marchal and Benoit. The dipole moments obtained from the measurements of the pure solute in both glycol series are discussed with reference to the Kirkwood g factor.

Dipole-moment measurements of polymer molecules can be used to obtain information on the relative orientation of the polar groups in the molecule and sometimes the ability of these groups to rotate. Polyethylene and polypropylene glycols, HO·[CH$_2$·CH$_2$·O]$_n$·H and HO·[CH$_2$·CHMe·O]$_n$·H, respectively, have a large degree of molecular freedom; rotation of the ether linkage can take place giving rise to an absorption in the radio-wave region.[1] In initiating these dipole-moment studies it was hoped to ascertain the ease of rotation by comparing the experimental values of the dipole moments with those calculated for a free-rotation model[2] and for a model involving some steric hindrance.[3] The Kirkwood correlation factor g is a valuable measure of both inter- and intra-molecular forces in a polymer, and in the present investigation this factor has been evaluated, enabling dipole moments obtained from the solution to be compared with those for the pure solute.

Experimental and Results

Polyethylene glycols of molecular weight 200—4000 were obtained from Oxirane Ltd. Polypropylene glycols of molecular weight 1000—4000 were obtained from the Union Carbide Chemicals Company, except that of molecular weight 400 which was supplied by the Dow Chemical Company.

Dielectric constants of the polyethylene glycols were measured on an N.P.L. calibrated Hartshorn–Ward dielectric test set;[4] those of the polypropylene glycols were made on the Cole–Gross bridge mark II.[5] Refractive indexes were measured with an Abbé refractometer. Benzene was purified as described by Prosskauer *et al.*[6]

Results.—Dipole moments were evaluated for the pure solute from the dielectric constant and refractive index by using Kirkwood's equation:[7]

$$\frac{(2\varepsilon_0 + n^2)(\varepsilon_0 - n^2)9kTV}{\varepsilon_0(n^2 + 2)^2} = g\mu^2, \qquad (1)$$

where ε_0 is the static dielectric constant of the solute, n is the refractive index, g is the Kirkwood correlation factor, and μ is the dipole moment of the molecule.

For solutions the dipole moment was calculated by Guggenheim's method:[8]

$$\frac{9kT}{4\pi N} \cdot \frac{3}{(\varepsilon_1 + 2)(n_1^2 + 2)} \cdot \frac{\Delta}{C} = \mu^2, \qquad (2)$$

where Δ is $(\varepsilon_0 - n_0^2) - (\varepsilon_1 - n_1^2)$, ε_0 is the static dielectric constant of the solution, n_0 is its

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refractive index, ε_1 is the static dielectric constant of the benzene, and n_1 is its refractive index. C is the concentration of the solute in moles per c.c. of solution.

TABLE 1.

Polyethylene glycols at 20°.

		Solute alone					In C_6H_6	
M	n	ε	$g\mu^2/n$ from eqn. 1	$g\mu^2$	g‡ from eqn. 3	μ (D)	μ (D)	μ^2/n
62	1	41·82 *	13·0	13·0	1·31	3·2	2·0	4·0
106	2	31·69 *	6·1	12·3	1·35	3·0	2·3	2·6
150	3	23·69 *	5·8	17·3	1·50	3·4	2·5	2·1
200	4	21·1	4·9	20·1	1·61	3·5	2·8	1·9
238	5	18·16 *	4·1	20·8	1·69	3·5	3·0	1·8
282	6	16·00 *	3·6	21·4	1·74	3·5	3·2	$1·7_6$
300	6·4	15·9	3·4	22·0	1·75	3·5	3·3	1·7
326	7	14·85 *	3·3	22·9	1·77	3·6	3·4	$1·6_7$
400	8·7	13·7	2·9	25·7	1·81	3·8	3·7	1·6
800	17·7	11·2	2·5	44·7	1·90	4·8	4·9	1·3
1000	22·2	10·9	2·4	54·4	1·92	5·3	5·3	$1·2_8$
1500	33·6	10·8	2·4	80·3	1·94	6·4	6·4	1·2

* By use of values given by Koizumi and Hanai (*J. Phys. Chem.*, 1956, **60**, 1496). † By use of values from ref. 3. ‡ Calculated by using $2\theta = 110°$.

TABLE 2.

Polypropylene glycols at 25°.

		Solute alone					In C_6H_6			
M	n	ε	$g\mu^2/n$ from eqn. 1	$g\mu^2$	g ‡ from eqn. 3	μ (D)	μ (D) from eqn. 2	μ^2/n	μ^{2*}/n	μ^2/n †
400	6·6	8·86	2·66	17·6	1·40	3·5	3·6	$1·9_6$	$1·9_6$	$2·2_6$
1000	17·2	6·16	1·6	27·7	1·56	4·2	4·8	$1·3_4$	$1·3_5$	$1·9_4$
2000	34·5	5·51	1·4	47·2	1·61	5·4	6·3	$1·1_4$	$1·1_4$	$1·8_0$
3000	51·7	5·27	1·3	66·2	1·63	6·4	7·6	$1·1_1$	$1·0_8$	$1·7_8$
4000	69·0	5·27	1·3	88·3	1·65	7·3	8·5	$1·05_3$	$1·0_7$	$1·7_8$

* By use of Marchal and Benoit's equation.[3]. † By use of Uchida *et al.*'s equation.[2] ‡ By using $2\theta = 120°$ (cf. text).

Table 1 contains the results for pure polyethylene glycol and Marchal and Benoit's results [3] for benzene solutions. Table 2 contains results, for both solute and solution, for polypropylene glycols.

DISCUSSION

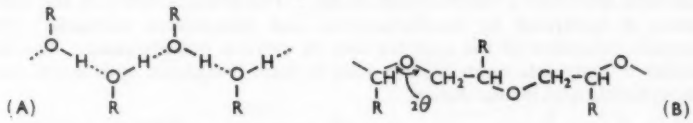
Solution Measurements.—Marchal and Benoit [3] and Uchida and his co-workers [2] put forward theoretical expressions whereby the dipole moments of polyethylene glycols and closely related structures may be calculated. Uchida *et al.* used a free-rotation model; Marchal and Benoit used a model incorporating a steric-hindrance factor which takes short-range interactions into account. In their work on the polyethylene glycols in dioxan, Uchida *et al.* measured the dipole moments of the polymers up to the heptamer, but even this comparatively small increase in molecular weight caused divergence between their experimental and theoretical values of the dipole moment, this being attributed to the " excluded volume effect." On the other hand, Marchal and Benoit measured the dipole moments of the polyethylene glycols in benzene up to a degree of polymerisation of 230 and found that their theoretical expression reproduced the experimental results very well. They also concluded that the " excluded volume effect " does not refer to polymer chains of this type.

In the present study the measured dipole moments agreed extremely well with Marchal and Benoit's theoretical expression, as shown in the last three columns of Table 2. This expression also reproduces the experimental values obtained by Uchida *et al.* for some polyethylene glycols in dioxan better than the expression which they themselves proposed (these calculations are not reported here).

Although the dielectric absorption data [1] indicate a remarkable freedom of rotation, the fact that a steric hindrance factor must be introduced to obtain agreement between the calculated and the experimental dipole moments indicates that freedom of rotation is not complete. This agrees with recent viscosity measurements [9] which show that polyethylene glycol maintains, in toluene solution, a very close configuration involving considerable hindrance to rotation. The value of 0·33 used for the steric-hindrance factor is a little larger than that (0·3) used by Marchal and Benoit in their work on the polyethylene glycols in benzene: it can be reasonably understood on the assumption that the methyl side chain in the polypropylene glycols hinders rotation about the ether linkage.

Measurements for Solutes.—Values of the dipole moment have been obtained from the measurement of the dielectric constants of the pure glycols by using equation 1, which gives values of the product $g\mu^2$ (see the fifth column of Tables 1 and 2). Kirkwood's correlation factor g is a measure of the degree of interaction between the many dipoles present in the dielectric. In the present context it is a measure of the interaction between the dipoles forming the randomly orientated polymer chain. To obtain values of the dipole moment μ from the product $g\mu^2$, values of g must be assumed.

In relatively simple cases, g can sometimes be successfully evaluated from X-ray data, but in such complex cases as liquid polymers this is not feasible. Oster and Kirkwood [10] adopted a rough model for the calculation of g for infinite chains of hydrogen-bonded aliphatic alcohols. This model was subsequently modified by Dannhauser and Cole [11] who adopted a model (A) composed of finite chains and obtained an expression for g in the



following manner. The value of g is different for different members i of a finite chain and a mean value is obtained and defined as $ng = \sum_i g_i$, where n is the number of alcohol molecules in the chain. If 2θ is the bond angle, which is assumed equal to the angle between the hydrogen bonds, then

$$g = 1 + 2f\cos^2\theta - \frac{2f\cos^2\theta \,.\, (1 - \cos^{2n}\theta)}{n\sin^4\theta},$$

where $f = (\mu_H + \mu_R)(\mu_H + \mu_R\cos 2\theta)/(\mu_H^2 + \mu_R^2 + 2\mu_H\mu_R\cos 2\theta)$; here μ_H and μ_R are the group moments.

This treatment has been used to evaluate g in the present investigation. In the place of fluctuating hydrogen-bonded chains we have permanent polymer entities involving covalent bonds. The model is thus (B), where R is a hydrogen atom in the polyethylene glycols and is methyl in the polypropylene glycols. 2θ is taken as the bond angle of the ether linkage. The values assumed for 2θ are given in Tables 1 and 2. The value of f is unity since the group moments corresponding to μ_H and μ_R are both μ_{O-O}.

The values of g calculated in this way are tabulated in the sixth column of Tables 1 and 2. From these and the values of $g\mu^2$, values of μ are obtained and may be compared with the dipole moments obtained from the solution measurements. This comparison is made in the seventh and the eighth column of the Tables. The agreement between the solution and solute dipole moment is striking, especially in the polyethylene glycol series. The poorer agreement for polypropylene glycols could be due to neglect of the definite contribution of the methyl side chain to the dipole moment of the polymer molecule.

[9] Thomas and Charlesby, *J. Polymer Sci.*, 1960, **42**, 195.
[10] Oster and Kirkwood, *J. Chem. Phys.*, 1943, **11**, 175.
[11] Dannhauser and Cole, *J. Chem. Phys.*, 1955, **23**, 1762.

However, the good agreement between the dipole moments from the two series of measurements indicates that the relatively simple model assumed for the polymer molecule is capable of giving realistic values of g.

Conclusion.—Marchal and Benoit's model, involving hindered rotation in the polymer chain, accurately represents the behaviour of both series of glycols in solution while the model given by Uchida *et al.* is in error. Reasonable values of the Kirkwood correlation parameter are obtained from a simple model of the polymer molecule, enabling values of the dipole moment to be obtained which are in good agreement with those for solutions.

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934. *Tungstate and Molybdate Complexes with Glycollic and Mandelic Acid.*

By D. H. BROWN.

Tungstate and molybdate ions form 1 : 2 complexes with glycollic and mandelic acid over a limited range of pH. The stoicheiometry of the complexes is confirmed by conductometric and polarimetric methods. The possible structures of the complex ions in solution are discussed. The inability of tungstate or molybdate ions to form complexes with acetic and phenylacetic acid is also shown.

COMPLEXES of α-hydroxy-carboxylic acids with tungstate, molybdate, and other inorganic anions have been known for some time.[1] In particular, Richardson [2] examined the stoicheiometry of the mandelic acid–molybdic acid and mandelic acid–tungstic acid complexes by conductometric methods, in acid solution. He claimed a 2 : 1 ratio for the former and a 3 : 1 ratio for the latter. The purpose of the present investigation was to confirm the stoicheiometry and to determine the nature of the complexes formed in solution by tungstate and molybdate ions with mandelic and glycollic acid.

EXPERIMENTAL AND RESULTS

Complexes of tungstate and molybdate with organic acids exist, in general, in weakly acid, neutral, and weakly alkaline solution, *i.e.*, at pH's where polymerisation of the simple anions normally occurs. Thus it can be difficult to determine whether complexes are formed and, if so, what is their nature, by conductometric or potentiometric methods involving a change in pH unless the species of tungstate or molybdate ion involved in the complex is known. Quantitative ultraviolet-absorption measurements are also confusing, as complex-formation and polymerisation cause similar shifts in the maxima.[2,3] In addition, the ultraviolet spectra of some of the 12-acids change with pH.[4] However, with some optically active organic compounds, a large increase in optical rotation is obtained when a complex is formed with tungstate or molybdate ion.[5] For L-mandelic acid, a plot of optical rotation against molar fraction of acid indicated a 2 : 1 mandelic acid : metal complex for both tungstate and molybdate (Fig. 1). Conductimetric measurements obtained on adding 10M-mandelic acid to 10^{-2}M-sodium tungstate confirmed the stoicheiometry (Fig. 2). The pH of these solutions changed, during the conductimetric titrations, from ~7·5 to ~3·0. In this pH range polymerisation of the tungstate ion

[1] Rimback and Ley, *Z. phys. Chem.*, 1922, **100**; Fairbrother and Taylor, *J.*, 1956, 4946.
[2] Richardson, *J. Inorg. Nuclear Chem.*, 1960, **13**, 84.
[3] Lindquist, *Acta Chem. Scand.*, 1951, **5**, 568; Cannon, *J. Inorg. Nuclear Chem.*, 1959, **9**, 252.
[4] Keller, Matigeric, and Kerker, *J. Phys. Chem.*, 1961, **65**, 56.
[5] Britton and Jackson, *J.*, 1934, 1055; Baillie and Brown, *J.*, 1961, 3691.

would certainly have competed with complex-formation unless the latter had been dominant. There was no break in the curves at $\frac{7}{6}$ equivalents of added hydrogen ion: this suggested that little paratungstate ion was formed. The reactions of the mandelatotungstate ion solutions also

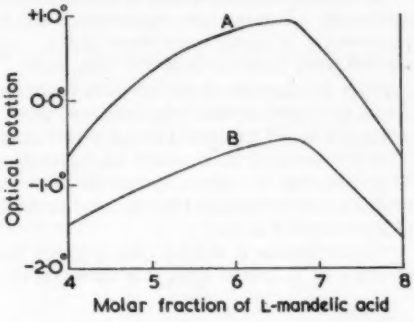

FIG. 1. Optical rotation plotted against molar fraction of L-mandelic acid.

(A) 2×10^{-2}M-Sodium molybdate and 2×10^{-2}-M-L-mandelic acid. (B) 2×10^{-2}M-Sodium tungstate and 2×10^{-2}M-L-mandelic acid.

supported the relative absence of polymerisation; *e.g.*, at pH 5·3 barium paratungstate was precipitated rapidly when barium chloride solution was added to 0·001M-paratungstate whereas if an excess of mandelic acid was present the precipitate was that of the complex. This value for the tungstate–mandelic acid complex is different from that obtained by Richardson.[2] He,

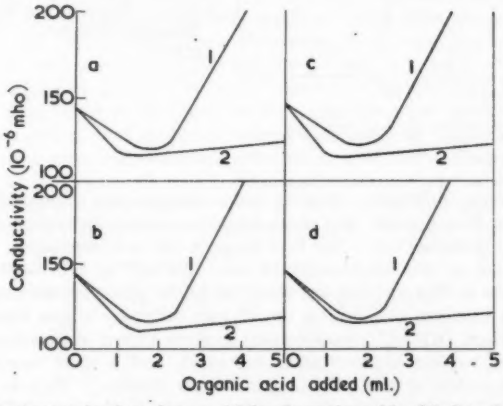

FIG. 2. Conductometric titrations. 10^{-1}M-Organic acid added to 10^{-3}M-inorganic salt solution (100 ml.).

a, (1) Mandelic acid–sodium tungstate. (2) Phenylacetic acid–sodium tungstate. b, (1) Glycollic acid–sodium tungstate. (2) Acetic acid–sodium tungstate. c, (1) Mandelic acid–sodium molybdate. (2) Phenylacetic acid–sodium molybdate. d, (1) Glycollic acid–sodium molybdate. (2) Acetic acid–sodium molybdate.

however, started with tungstic acid of unknown molecular weight, in solution at a pH <2, where, as judged from Fig. 3, polymerisation of the tungstate ions competes with complex-formation.

To determine the range of stability of the L-mandelato-tungstate and -molybdate complexes, the optical rotations for solutions of a fixed concentration at different pH values were found (Fig. 3) (20 cm. tube; sodium D light). They show that complex-formation on the alkaline side begins around pH 8·8 for the tungstate complex and around pH 7·6 for the molybdate complex. In both cases the region of maximum optical rotation occurs in the region of pH 3—5. Below this pH range, presumably, the competing reaction of tungstate or molybdate polymerisation had a greater effect, and above it the complexes are hydrolysed. The greater change in

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the optical rotation with the molybdate than with the tungsten complex is probably due to the smaller size of the molybdenum(VI) ion, causing a greater electron shift away from the asymmetric carbon atom towards the metal ion.

Potentiometric titration of solutions of mandelato-molybdate and -tungstate with sodium hydroxide solution show equivalence points around pH 7·6 and 8·6, respectively, after two equivalents of alkali have been added. These values correspond to those mentioned above for complete hydrolysis of the complexes. Thus complete neutralisation of the acid present appears to correspond to complete hydrolysis of the complexes. This will be the case if the acidic hydrogen in the carboxylic acid group is involved in the complex-formation. The initial steep rise in pH between 4·3 and 6 corresponds to part of the region of approximately constant optical rotation (Fig. 3) where the concentration of the complexes appears to be fairly constant. Thus addition of sodium hydroxide causes a rapid increase in pH until the hydroxyl ion concentration is sufficiently high to cause hydrolysis of the complexes with subsequent neutralisation of the liberated acids.

To determine if the α-hydroxy-group was involved in the complex, phenylacetic was used in place of mandelic acid, the dissociation constants 3·41 for mandelic acid [6] and 4·31 for

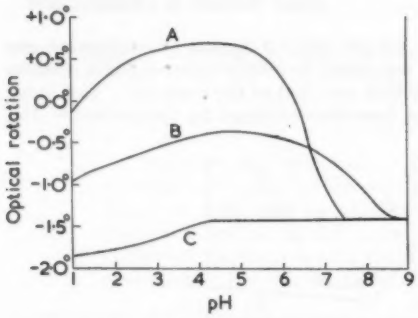

FIG. 3. Optical rotation plotted against pH.

A, 0·02M-L-Mandelatomolybdate. B, 0·02M-L-Mandelatotungstate. C, 0·02M-L-Mandelic acid.

phenylacetic acid [7] being sufficiently close to make comparisons reasonably valid. Conductometric titrations (Fig. 2) suggested that there was no complex-formation and that the turning points were due to polymerisation. The first stage in the polymerisation of the tungstate ion involves the formation of the paratungstate ion: $6WO_4^{2-} + 7H^+ \rightleftharpoons HW_6O_{21}^{5-} + 3H_2O$. The turning points due to this reaction are observed in the phenylacetic and acetic acid graphs. Further acidification involves the taking up of two other hydrogen ions to give the anion $H_3W_6O_{21}^{3-}$. This stage, although characterised to some extent in titrations with hydrochloric acid, is masked when weaker organic acids are used, and a slow increase in conductivity due to the buffering action of the polytungstate ions results. This is in contrast to the rapid increase of conductivity after the turning point in the mandelic and glycollic acid graphs. Here, after all the tungstate has been converted into complex, the increase in conductivity is due to the addition of the organic acid. Similar conclusions can be drawn from the molybdate titrations. These results were confirmed by adding phenylacetic acid to a standard solution of D-tartratotungstate and comparing the optical rotation with that of a similar solution with dilute hydrochloric acid in place of the phenylacetic acid, both solutions being adjusted to pH 4. There was no change in the optical rotation even when a large excess of phenylacetic acid was used. Similar results were obtained on use of D-tartratomolybdate. Thus it seems that phenylacetic acid does not form a complex with tungstate or molybdate ions or, if it does, the complex formed is very weak and cannot compete with the normal polymerisation.

To confirm this effect of the α-hydroxy-group acetic and glycollic acid were also compared. Again conductometric evidence (Fig. 2) suggested that glycollic acid formed a 2 : 1 complex with both molybdate and tungstate ions and that acetic acid did not. This was confirmed, as above, by measuring the effect on the optical rotation of D-tartrato-tungstate and -molybdate solutions at pH 4. Glycollic acid in both cases lowered the optical rotation whereas acetic

[6] Banks and Davies, *J.*, 1938, 73.
[7] Lloyd, Wycherley, and Monk, *J.*, 1951, 1786.

acid had no effect. Since the optical rotation of D-tartratotungstate solution is proportional to its concentration, the use of known initial concentrations of D-tartratotungstate and glycollic acid and measurement of the resulting optical rotation of the solution permits the concentration of D-tartratotungstate and hence the equilibrium constant for the following equation to be calculated:

$$\text{D-Tartratotungstate} + C \times \text{Glycollic acid} \rightleftharpoons \text{Glycollatotungstate} + \text{D-Tartaric acid}$$

where C is an integral constant. By using various concentrations of glycollic acid, a constant value for the equilibrium constant was found for $C = 2$. The values for $C = 1$ are given for comparison (Table; 20°; pH 4·0). A similar result was found for the glycollatomolybdate complex. These results confirm the 1 : 2 stoicheiometry.

Glycollic acid, orig. concn. (M)	D-Tartratotungstate orig. concn. (M)	D-Tartratotungstate final concn. (M)	K for $C = 1$	K for $C = 2$
0·050	0·040	0·028	0·135	7·63
0·060	0·040	0·026	0·168	7·42
0·070	0·040	0·024	0·197	7·41
0·080	0·040	0·022	0·238	7·64

The silver salts of the mandelato- and glycollato-tungstate complexes were prepared and the infrared spectra measured (potassium chloride discs). These salts were dibasic and had the general formula Ag_2WO_4(organic acid)$_2$. Their spectra were compared with those of the corresponding free acids and normal silver salts. The carbonyl peak for the free acids, the normal salts, and tungstate complexes were at 1725, 1580, and 1630 cm.$^{-1}$, respectively. These figures suggested that the carbonyl group was involved in complex-formation. Similar results were obtained for the molybdate complexes. There was no apparent change in the wavelength of the hydroxyl peak at 3400 cm.$^{-1}$ though it appeared relatively much stronger in the complex than in the normal salts. Since the free acid showed hydrogen-bonded hydroxyl groups, this confirmed the view that those in the complex were also hydrogen-bonded.

The silver content of the salts described above was found by dissolving the salts in dilute nitric acid, precipitating silver with sodium chloride, and drying and weighing the precipitate. After the silver had been removed, cinchonine hydrochloride was added to precipitate the tungstate or molybdate complex which was then filtered off and ignited to WO_3 or MoO_3. The organic acid content was found by standard analysis. Typical results are:

	Found (%)				Required (%)		
Ag salt	Ag	MO_4	Org. acid	Formula	Ag	MO_4	Org. acid
Mandelatotungstate	28·7	32·4	39·4	$Ag_2WO_4(C_8H_7O_3)_2$	28·1	32·3	39·6
Glycollatotungstate	35·3	40·5	24·5	$Ag_2WO_4(C_2H_3O_3)_2$	35·1	40·3	24·7
Mandelatomolybdate ...	31·9	23·7	44·6	$Ag_2MoO_4(C_8H_7O_3)_2$	31·8	23·5	44·7
Glycollatomolybdate ...	50·1	30·4	28·6	$Ag_2MoO_4(C_2H_3O_3)_2$	40·9	30·3	28·8

The ethyl esters of the four organic acids were prepared. However, even when added in large excess to solutions of D-tartratotungstate (or molybdate), they did not alter the value of the optical rotation from that observed in a solution acidified to the same pH with hydrochloric acid, thus showing their inability to form complexes. This evidence also suggests that the hydroxy-group of the carboxylic acid is involved in the complex.

Discussion

Our evidence indicates that mandelic and glycollic acid form 2 : 1 complexes with molybdate and tungstate ions whereas phenylacetic and acetic acids do not. Also, since the carbonyl and two hydroxy-groups are involved in the complex, the un-ionised organic acid appears to be the complex-forming ligand. The state of the tungstate and molybdate ions is more difficult to confirm. Analyses of the solid salts of the complexes suggest that the complex-forming species are the normal molybdate and tungstate ions. Since no change in pH occurs on precipitation, there appears to be no depolymerisation of polytungstate or polymolybdate. Some qualitative evidence can also be obtained from the change in pH obtained on mixing solutions of sodium tungstate and mandelic acid, both

being adjusted to the same initial pH (6·2) where the main species are paratungstate and mandelate: the pH of the resulting mixture was 6·9. After an initial pH of 2·2, the main species being the more acidic forms of the paratungstate ion and mandelic acid, the pH of the mixture was 1·8. In the first case, the increase in pH is probably due to uptake of hydrogen ion to give the un-ionised mandelic acid which is the complex-forming species. This is partly compensated by the hydrogen ions produced by depolymerisation of the polytungstate ions. In the second case, the decrease in pH can only be due to depolymerisation of polytungstate.

Optical-density measurements also gave some indication of the nature of the complex-forming metal anion. The optical densities of 10^{-4}M-solutions of sodium tungstate, sodium paratungstate, sodium glycollatotungstate, and glycollic acid at 240 mμ were 0·05, 0·30, 0·11, and 0·04, respectively, which suggests that the complex-forming species was the normal tungstate and not the paratungstate ion.

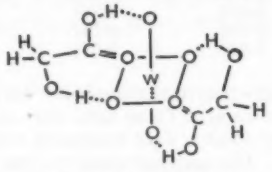

FIG. 4. Possible structure for the glycollatotungstate ion.

In most tungstate and molybdate structures so far confirmed, a central metal ion surrounded octahedrally by six oxygen ions is the basic building unit.[9] If we assume for the glycollatotungstate ion an octahedral structure around the central tungsten atom, then a possible structure might be that shown in Fig. 4. This includes a six- and a seven-membered ring, both involving relatively weak hydrogen bonding and both necessary for stability of the complex. A similar structure can be drawn for the glycollatomolybdate ion and for the corresponding mandelic acid complexes.

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GLASGOW, C.1.

[*Received, April 28th,* 1961.]

[8] Souchay, *Ann. Chim.* (*France*), 1943, **18**, 169.
[9] Keggin, *Proc. Roy. Soc.*, 1934, *A*, **144**, 75; Brown and Mair, *J.*, 1958, 2597; Waugh, Shoemaker, and Pauling, *Acta Cryst.*, 1954, **7**, 438.

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935. *High-resolution Nuclear Magnetic Resonance Spectra of Pentafluorosulphur Compounds.*

By R. K. HARRIS and K. J. PACKER.

The ^{19}F nuclear magnetic resonance spectra of pentafluorosulphur phenoxide, SF_5OPh, and chloride, SF_5Cl, were examined as examples of the AB_4 nuclear magnetic system with markedly different values for the ratio of the coupling constant, J_{AB}, to the chemical shift, δ_{AB}. The nuclear magnetic resonance spectrum of a newly prepared molecule, probably $SF_5{\cdot}O{\cdot}SO_2F$, was consistent with that of an AB_4X system.

THE pentafluorosulphur (SF_5) group contains two different types of fluorine atom. The stereochemistry is based on a pyramid, and the unique atom at the apex is known as the axial fluorine. The other four fluorine atoms are stereochemically and magnetically equivalent, and are said to be equatorial; thus the SF_5 compounds studied in this work give spectra characteristic of the AB_4 nuclear magnetic system.[1] This system has been

[1] Pople, Schneider, and Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., New York, 1959.

studied theoretically by several authors,[2,3] usually using the symmetry properties to simplify the Hamiltonian. The theory has been applied to perfluoroalkyl derivatives of SF_6 containing the SF_5 group by Muller, Lauterbur, and Svatos.[4]

Experimental.—Pentafluorosulphur fluorosulphonate, $SF_5{\cdot}O{\cdot}SO_2F$, was obtained by photochemical reaction of disulphur decafluoride with sulphur dioxide.[5] The infrared spectrum in the range 4000—400 cm.$^{-1}$, the ^{19}F nuclear magnetic resonance spectrum, the molecular weight, and chemical analysis are consistent with the above formulation. The other two compounds were kindly supplied by Imperial Chemical Industries Limited, Alkali Division.

The spectra were obtained at 40 Mc./sec. by using a Varian Associates V4300A nuclear magnetic resonance spectrometer and 12" electromagnet with flux stabilisation, sample spinning, and a Varian V4365 field homogeneity control unit. The compounds were dissolved in trichlorofluoromethane and sealed under a vacuum in Pyrex tubes of 5 mm. outside diameter. The concentrations obtained were ~80% by volume for pentafluorosulphur phenoxide, 60% for the chloride, and 16% for the fluorosulphonate. Positions of the unshifted A and B resonances are quoted relative to trichlorofluoromethane.[6] The separations between lines were measured by using side-bands of the compounds themselves, generated by a Muirhead–Wigan D695A decade oscillator. The sweep-rate was somewhat variable at the time that the measurements were made, so that line positions, and the parameters obtained, have the accuracies quoted in Tables 1 and 2. The values are, however, sufficiently accurate for a valid comparison of observed and calculated line positions.

Theoretical Considerations.—In this laboratory, the AB_4 system has been analysed by the "complex particle" method of Whitman *et al.*[7] Details of this analysis will be published later.[8] The basis of the method is that wave functions which are eigenfunctions of I_A^2 or I_B^2 (where I is the total spin angular momentum operator of the group designated) do not mix. The states with $J = 0$, $\frac{1}{2}$, 1, $\frac{3}{2}$, and 2 (where J is the eigenvalue of I) are known as singlet, doublet, triplet, quartet, and quintet states, abbreviated to S, D, T, Q, and Qt, respectively. Here the A group has only the D state, but the B group can occur in S, T, or Qt states. The possible overall states for this system are therefore D_AS_B, D_AT_B, and D_AQt_B. These have degeneracies 2, 3, and 1, respectively.[7,8] The matrix representing the Hamiltonian for each state can be written down, and the corresponding frequencies and intensities of transitions calculated separately.[7,8] The degeneracy factor means that DT lines are normally more intense than the others. The appearance of the spectrum (apart from scaling factors) depends solely on the ratio, R, of the coupling constant, J_{AB}, to the chemical shift, δ_{AB}.

The spectra were assigned by a calculation in which an estimated value of R was used. The values of J_{AB} and δ_{AB} can then be measured separately and directly by using the DT and DS lines. The single DS line is at the unshifted resonance of the A nucleus, while lines 23 and 20, 19 and 16, 7 and 4, and 15 and 12 are symmetrically placed about the resonance position of the B nuclei,[9] the first-mentioned line in each case being that nearer to the A lines. The line notation is that of ref. 8, and as denoted in the Figures. Since lines 7 and 4 are sharper than the others (originating from DT state), and also clearly resolved for pentafluorosulphur phenoxide and fluorosulphonate, their centre was used as the unshifted resonance of the B nuclei. The chemical shift between the A and B nuclei was obtained by the equation

$$|\delta_{AB}| = E_1 - E_7 + \tfrac{1}{2}(E_7 - E_4),$$

where E_i is the position in cycles/sec. of the ith line. The coupling constant can be

[2] Banerjee, Das, and Saha, *Proc. Roy. Soc.*, 1954, *A*, **226**, 490.
[3] Corio, *Chem. Rev.*, 1960, **60**, 363.
[4] Muller, Lauterbur, and Svatos, *J. Amer. Chem. Soc.*, 1957, **79**, 1043.
[5] Emeléus and Packer, unpublished work.
[6] Filipovich and Tiers, *J. Phys. Chem.*, 1959, **63**, 761.
[7] Whitman, Onsager, Saunders, and Dubb, *J. Chem. Phys.*, 1960, **32**, 67.
[8] Chapman, unpublished work.
[9] Harris, unpublished work.

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obtained by direct measurement from several different sets of four or five lines from the DS and DT states, the equations concerned involving no square-root terms. The most convenient proved to be:

$$3|J_{AB}| = 2(E_8 - E_3) - (E_7 - E_4).$$

Once J_{AB} and δ_{AB} have been measured, the complete spectrum can be calculated from the accurate value of R, and compared with the observed spectrum.

Pentafluorosulphur Phenoxide, $SF_5{\cdot}OPh$.—In this case the five-line A spectrum of the AX_4 case has been perturbed to give the theoretical nine lines of the AB_4 case. Likewise, the doublet characteristic of the X nuclei of the AX_4 case has split to give twelve lines. All 21 lines are clearly visible (Fig. 1), but none of the four combination lines is of sufficient intensity to be seen (calculations show that the strongest of these has only 2% of the intensity of the DS line). A value of R of 0·35 was estimated from the spectrum, and an approximate calculation quickly gave the assignment of the lines in the correct order, and with the expected intensity ratios. It can be seen that line 13 has crossed line 1 from its AX_4 position—this is the only example of such a crossing in the three molecules studied. Lines 1,3,4,7,and 8 were then used to measure J_{AB} and δ_{AB} directly. The complete calculated and observed spectra were in good agreement (Fig. 1 and Tables 1 and 2). The resonance of the equatorial fluorine nuclei occurred to high-field side of the axial nucleus; this is true also for the molecule $SF_5{\cdot}CF_2{\cdot}CF_3$ studied by Muller, Lauterbur, and Svatos,[4] but the opposite result is found for our chloride and fluorosulphonate.

Pentafluorosulphur Chloride, SF_5Cl.—The chemical shift, δ_{AB}, is here much greater than the coupling constant, so that the spectrum is much closer to the AX_4 case than is that of the phenoxide. Nevertheless, all nine lines of the A spectrum are clearly resolved (Fig. 2a). In the B spectrum, however, the lines overlap, so that each line of the original AX_4 doublet appears as a broad quartet (Fig. 2c). R was estimated at 0·06, and a calculation gave the assignment of the lines, as for the phenoxide. This shows that the four most intense peaks in the B spectrum can be assigned partly to the DT lines 7, 9, 4, and 2 (in order of proximity to the A lines), as expected by comparison with the phenoxide. The exact values of J_{AB} and δ_{AB} were then obtained by direct measurement as before.

Pentafluorosulphur Fluorosulphonate, $SF_5{\cdot}O{\cdot}SO_2F$.—This compound has only recently been prepared, and its identity was decided partly by its nuclear magnetic resonance spectrum. The nuclei form an AB_4X system, the chemical shift of the X nucleus (the fluorine of the SO_2F group) from A and B being very large compared with its coupling constants to these nuclei (Table 3). J_{AX} is small (~0·9 cycle/sec.) and, since the separations in the A spectrum are large, this splitting caused no complications. In the B spectrum, however, the splitting from X ($7{\cdot}2 \pm 0{\cdot}2$ cycles/sec.) causes lines to overlap, but it is still no difficult matter to give a complete assignment (Fig. 3). The X spectrum occurs to high-field side of the A lines, and consists of a pentet of doublets, in accordance with the simplified theory. The AB_4 spectrum could be assigned by comparison with the phenoxide, and the values of J_{AB} and δ_{AB} measured as before. The presence of the pentafluorosulphur group was confirmed by the value of J_{AB} (Table 3).

Line Widths.—The line widths at half-maximum height are not the same throughout the spectrum of a given molecule of the AB_4 type. It was found that the DS line is always much sharper than the others, and this fact can be useful in the original assignment of the spectrum. Also, the DT lines are distinctly sharper than the DQt lines, so that peak heights are not good guides to relative intensities. This is well seen in Fig. 1, where the height of line 2 (DT state) is appreciably greater than that of line 11 (DQt state), although the calculated intensities are almost equal.

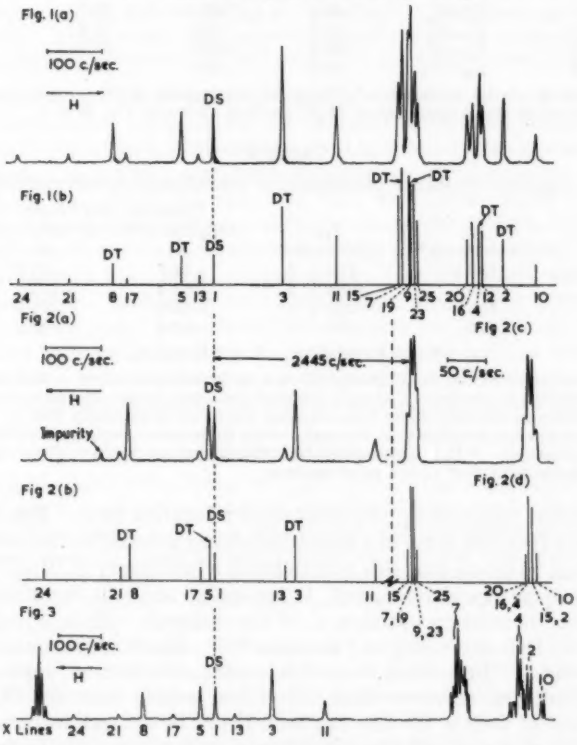
These observations cannot be explained by the effects of exchange processes or quadrupole relaxation, as in some other examples of line-width differences occurring in a single molecule.[10] Here the differences are probably due to the fact that DS, DT, and DQt

[10] Pople, *Mol. Phys.*, 1958, **1**, 168.

FIG. 1. (a) Observed and (b) calculated spectrum of $SF_5 \cdot OPh$.

FIG. 2. (a) Observed and (b) calculated A spectrum of SF_5Cl. (c) Observed and (d) calculated B spectrum of SF_5Cl.

FIG. 3. Observed spectrum of $SF_5 \cdot O \cdot SO_2F$.



In Fig. 1, *H* increases in the opposite direction from that of Figs. 2 and 3.

In Fig. 2, the scale of (c) and (d) is different from that of (a) and (b), both horizontally and vertically.

The unmarked lines in Figs. 1(b) and 2(b) arise from the DQt state.

The line numberings are in the notation of ref. 8.

The doublet splitting of the A and X lines of Fig. 3 cannot be observed on this scale.

The line heights are not directly proportiona lto line intensities owing to the rapid sweep rate.

TABLE 1.

A comparison of calculated and observed line separations [a] in the A spectrum.

The separations of the DQt lines from the unshifted A resonance are given in cycles/sec.

	$SF_5 \cdot OPh$		SF_5Cl		$SF_5 \cdot O \cdot SO_2F$ [b]	
Line no.	Calc.	Obs.[c]	Calc.	Obs.	Calc.	Obs.[c]
11	222·6	223	290·3	289	260·2	260
13	25·1	26	126·6	126	46·1	46·5
17	156·9	157	26·6	27	105·1	105
21	262·4	264	169·8	171	229·9	229
24	353·2	354	308·2	308	338·9	338

[a] Magnitudes given only. [b] The positions are for the centres of doublets produced by coupling the F atom of the SO_2F group. [c] ±1·5 cycles/sec.

TABLE 2.

Some calculated and observed line separations [a] in the B spectrum [d] in cycles/sec.

State	Line separations	$SF_5{\cdot}OPh$ Calc.	$SF_5{\cdot}OPh$ Obs.[c]	$SF_5{\cdot}O{\cdot}SO_2F$ [b] Calc.	$SF_5{\cdot}O{\cdot}SO_2F$ [b] Obs.[c]
DT	E_3—E_4	44·1	43·5	24·7	24·5
DT	E_9—E_7	14·6	14·5	12·2	12·0
DQt	E_{10}—E_4	103·6	103·0	56·2	56·0
DQt	E_{25}—E_7	26·6	26·6	22·5	22·5

[a, b] See Table 1. [c] ±1 cycle/sec. [d] Owing to overlapping lines, comparison of observed and calculated positions in the B spectrum of SF_5Cl are best shown in Fig. 2c & d.

TABLE 3.

Nuclear magnetic resonance parameters of pentafluorosulphur compounds.

Compound	J_{AB} (cycles/sec.) *	δ_{AB} (cycles/sec.)	Chemical shift [b] from CCl_3F in parts per million † A	B	$R(=J_{AB}/\delta_{AB})$
SF_5OPh	158·5	410 ± 2	−72·7	−62·6	0·386
SF_5Cl	150	2520 ± 5	−62·3	−125·2	0·0596
$SF_5{\cdot}O{\cdot}SO_2F$ [a]	156	650 ± 2	−55·6	−71·9	0·238
$SF_5{\cdot}CF_2{\cdot}CF_3$ [b]	145	752	−61·0	−42·2	0·193

* ±1·5 cycles/sec. † ±0·15 p.p.m.

[a] The fluorine atom of the SO_2F groups gives a spectrum centred at −45·1 p.p.m. from CCl_3F. The coupling constant to the axial F atom is 0·9 cycle/sec., and to the equatorial atoms 7·2 cycles/sec. The marked difference between these two coupling constants is probably due to the importance of direct terms (through space rather than through bonds) in fluorine couplings (Petrakis and Sederholm, private communication). [b] It is noteworthy that the resonance position of the equatorial nuclei is much more variable than that of the axial nucleus.

states have different values of T_1, the spin-lattice relaxation time. This time T_1 depends on the probability (per unit time) of a transition's being induced by the random perturbing field, $H(t)$. It can be shown that this probability is a function of $\langle\psi_2|H|\psi_1\rangle^2$ for a transition from eigenstate ψ_1 to eigenstate ψ_2 (ref. 1, appendix) and will therefore vary with the total spin angular momentum operator, I, of the molecule. Thus, T_1 will differ for the states DS, DT, and DQt, decreasing as I increases.[11,12] This would account for the observed line-width differences. In general, in an AB_n system, if n is even, there will be a single line in the A spectrum, narrower than the others, arising from the D_AS_B state. The extreme sharpness of such a DS line has been noted by several authors.[7,11,13] For the A_mB_n system, this situation will occur if either m or n is even. If both are even, there will be such a line in both the A and the B part of the spectrum. These facts can be of great use in analysing such a spectrum, if the separate lines are resolved.

We are grateful to the Research Department of Imperial Chemical Industries Limited, Alkali Division, for generous gifts of pentafluorosulphur chloride and phenoxide, to Professor H. J. Emeléus and Dr. N. Sheppard for their interest and help, to Dr. E. A. V. Ebsworth for the original suggestion of completely analysing the spectra, to Dr. D. Chapman for useful discussions on the analysis, and to Mr. E. Liddell for running some of the spectra. Both of us are indebted to the Department of Scientific and Industrial Research for research studentships.

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[*Received, May 29th,* 1961.]

[11] Anderson and Arnold, *Discuss. Faraday Soc.*, 1955, **19**, 226.
[12] Abragam, "The Principles of Nuclear Magnetism," Oxford Univ. Press, 1961.
[13] Sheppard and Turner, *Mol. Phys.*, 1960, **3**, 168.

936. *Intracrystalline Oxidation of Hydrogen Sulphide.*

By W. E. Addison and Anne Walton.

Hydrogen sulphide reacts with oxygen within the channels of zeolites to form products which vary according to experimental conditions and to the zeolite used. Direct oxidation to sulphur trioxide occurs at a temperature of 100° c in molecular sieve 4A or at 200° in the calcium form of sieve 13X.

A number of reactions has been found to proceed in zeolitic channels and this illustrates that such an intracrystalline environment can promote unexpected chemical behaviour. Addison and Barrer [1] found that nitric oxide sorbed in zeolites disproportionates to form other nitrogen oxides, and, under conditions which prevent the complete disproportionation of nitric oxide, the sorbed gas does not react with subsequently sorbed oxygen. Beachell and John [2] found that sorption of diborane on several zeolites is irreversible and suggested that this was due to chemical reaction leading to the attachment of boron to the aluminosilicate framework by a boron–oxygen bond. Cannon [3] found that the sorption of chlorodifluoromethane in zeolites initiates a reaction in which carbon dioxide is formed. Further examples of unexpected intracrystalline behaviour are given in reference 1.

The oxidation of hydrogen sulphide within zeolitic channels has now been investigated and it has been shown that zeolites promote this oxidation and that the course of the oxidation depends upon both the particular zeolite used and the experimental conditions.

Experimental and Results

Oxygen was supplied pure by the British Oxygen Co. Ltd. Hydrogen sulphide was prepared by the action of dilute hydrochloric acid on zinc sulphide and was dried with calcium chloride and then fractionated until no impurity was detected in its infrared spectrum.

The zeolites used were the Linde molecular sieves 4A, 5A, and 13X and the calcium and potassium modifications of the last, prepared by treating the zeolite with saturated solutions of the appropriate metal chloride. Before being used for gas sorption each sample of zeolite was outgassed overnight at 300°/10^{-6} mm.

Gas sorption was measured by volumetric methods.

Method.—Hydrogen sulphide was admitted to the zeolite at 200° (after it had been demonstrated that no decomposition of hydrogen sulphide occurs under these conditions), and the whole was cooled to the appropriate temperature during 24 hr. before oxidation was started. This procedure should minimise the tendency for sorbate molecules to form clusters and should produce a more uniform distribution throughout the zeolite crystals.[4] The volume of hydrogen sulphide used was in all cases such that no pressure could be detected in the gas phase when equilibrium had been reached. Successive doses of oxygen were admitted to the system and each was left until no further change in pressure was detected during a period of 24 hr.

Results.—Runs were carried out at 0°, 100°, and 200° c with different zeolites and different concentrations of hydrogen sulphide within each zeolite. A considerably greater volume of oxygen was always sorbed than was expected by comparison with the same system in the absence of hydrogen sulphide. After 24 hr. at 100° and 200° no gas, and at 0° only a small volume of gas could be desorbed although the sorption of oxygen by zeolites is normally completely reversible. Some desorption could be effected by raising the temperature above 200°. These features indicate that chemical reaction took place between hydrogen sulphide and oxygen within the zeolitic channels. (Hydrogen sulphide and the possible products of its oxidation would be sorbed more strongly than oxygen and would not be desorbed readily.)

In Table 1 are presented the data for the two zeolites which have been studied most completely, *i.e.*, sieve 4A and the calcium form of sieve 13X. The ratio of the volume of oxygen sorbed to the volume of hydrogen sulphide pre-sorbed (v_{O_2}/v_{H_2S}) increases with increase of temperature and with decrease in the concentration of hydrogen sulphide within the sorbent.

[1] Addison and Barrer, *J.*, 1955, 757.
[2] Beachell and John, *J. Chim. phys.*, 1958, **55**, 280.
[3] Cannon, *J. Phys. Chem.*, 1959, **63**, 160.
[4] Barrer and Rees, *Trans. Faraday Soc.*, 1954, **50**, 852.

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Under comparable conditions the ratio v_{O_2}/v_{H_2S} is greater in sieve 4A than in the calcium form of sieve 13X.

TABLE 1.

H_2S sorbed per g. of zeolite (c.c. at N.T.P.)	Temp.	v_{O_2}/v_{H_2S} at p_{O_2} 0 cm.	70 cm.	H_2S sorbed per g. of zeolite (c.c. at N.T.P.)	Temp.	v_{O_2}/v_{H_2S} at p_{O_2} 0 cm.	70 cm.
	Sieve Ca13X				Sieve 4A		
14·29	0°	0·51	0·58	6·21	0°	0·93	1·01
16·53	100	0·46	0·65	5·03	100	1·65	1·70
15·46	100	0·49	0·64	1·17	100	1·24	2·00
4·32	100	0·67	0·89	1·08	200	1·95	1·95
1·12	100	0·80	1·13				
7·79	200	1·49	1·50				
3·80	200	1·61	2·00				
1·02	200	1·80	2·00				

In those runs in which some oxygen was desorbed, such a volume is considered to have been physically sorbed and the ratios quoted in the last column above have been corrected for this and represent the amount of chemisorption.

Values for v_{O_2}/v_{H_2S} are quoted for two different pressures of oxygen in the gas phase; by comparing the pairs of columns of Table 1 it can be seen that in each run at least 60% (and in many cases appreciably more) of the oxygen was sorbed before any pressure of gas could be detected in the gas phase. The pressure of 70 cm. was chosen to indicate the extent of reaction at a pressure which approximates to atmospheric.

Identification of Reaction Products.—Evidence of the products formed in the various reactions was obtained after completion of the oxidation by pumping off the excess of oxygen, hydrothermally extracting the zeolite, and testing the resultant solutions qualitatively. The results are shown in Table 2, and are for sieve 4A, except that for the ratio 0·58, which is for the calcium form of sieve 13X. When the zeolite was heated to effect complete desorption, gaseous sulphur dioxide was evolved where the ratio was $<2{\cdot}0$ and identified by measurement of its infrared spectrum. The presence of sulphur formed within the zeolitic channels as an oxidation product in samples where the ratio was between 0·5 and 1·0 has been inferred from two observations: first, that the zeolite after an oxidation experiment and subsequent outgassing showed a measurable paramagnetism that was not detected in the fresh zeolite; and, secondly, after the zeolite had been outgassed at 300° to remove any volatile products of reaction, further sorption of oxygen could be effected which was irreversible, appreciable in amount, and extremely slow; subsequent desorption on heating released sulphur dioxide which was detected as above.

The formation of sulphur as a product of the oxidation of hydrogen sulphide when a gaseous mixture was streamed over sieve 13X has recently been reported by Kerr and Johnson.[5]

TABLE 2.

v_{O_2}/v_{H_2S}	0·58	1·01	1·35	1·70	2·00
Test for SO_3^{2-}	+	+	+	+	−
SO_4^{2-}	−	−	+	+	+

DISCUSSION

Hydrogen sulphide can react with oxygen to give different products:

$$H_2S + \tfrac{1}{2}O_2 \longrightarrow H_2O + S \quad (1)$$
$$H_2S + O_2 \longrightarrow H_2O + SO \quad (2)$$
$$H_2S + \tfrac{3}{2}O_2 \longrightarrow H_2O + SO_2 \quad (3)$$
$$H_2S + 2O_2 \longrightarrow H_2O + SO_3 \quad (4)$$

The ratios of v_{O_2}/v_{H_2S} obtained when these reactions proceed stoicheiometrically are 0·5, 1·0, 1·5, and 2·0, respectively. The ratios obtained in the oxidation experiments seldom correspond with these ideal values and such a ratio is no guide to the products which have been formed, unless it be 2·0; in that case sulphur trioxide must have been formed quantitatively in accordance with reaction (4) since no further oxidation, and thus

[5] Kerr and Johnson, *J. Phys. Chem.*, 1960, **64**, 381.

greater ratio, can occur. If the ratio in a given experiment were 1·5, this could mean that 75% of the hydrogen sulphide molecules had reacted completely to form sulphur trioxide while the remaining 25% did not react at all, or that 100% of the molecules had reacted to form either sulphur dioxide or a mixture of sulphur, sulphur dioxide, and sulphur trioxide.

Since an appreciable quantity of sulphur dioxide was detected in a sample on which the ratio of 0·58 was obtained, and an appreciable amount of sulphur trioxide for a ratio of 1·35, it is clear that reaction does not proceed in such a way that reaction (1) above is complete before reaction (2) commences, etc. Further evidence of this was obtained by treating hydrogen sulphide in a zeolite with oxygen under conditions which had been shown to lead to complete formation of sulphur trioxide, but now only half the required volume of oxygen was admitted. A considerable amount of sulphate was detected after hydrothermal extraction.

It is postulated that the initial step in the intracrystalline reaction is the bimolecular one (2), since it is unlikely that any zeolitic cage could contain more than two molecules under the conditions used. There is evidence that when hydrogen sulphide is sorbed in sieve 4A one molecule is situated at the centre of a cage in the aluminosilicate framework,[6] and it seems likely that a similar situation could apply to sieve 13X. Under conditions which cause the sorbed species to have a low mobility, the molecules of water and sulphur monoxide formed in the initial reaction would remain in the one cage; this would prevent the access of a further oxygen molecule to react with the molecule of sulphur monoxide and lead to further oxidation. When several cages have become blocked by molecules of the reaction products in this way the access of a first molecule of oxygen to some cages which contain hydrogen sulphide molecules would be prevented. (The effect of water molecules in decreasing the sorption capacity of zeolites has been discussed by Barrer.[7]) Thus the complete oxidation of hydrogen sulphide to this stage resulting in the overall ratio of 1·0 is not reached. The prevention of complete reaction would be more likely the higher the concentration of presorbed hydrogen sulphide in the zeolite, since the number of blocked cages must be related to the number of hydrogen sulphide molecules present. The v_{O_2}/v_{H_2O} ratio can be seen always to decrease with an increase in the amount of presorbed hydrogen sulphide when other conditions are maintained constant (Table 1).

When no attempt was made to distribute hydrogen sulphide uniformly, as described above, the volume of oxygen taken up under otherwise comparable conditions was reduced. The higher local concentrations of hydrogen sulphide molecules would make it more possible for blocked cages to stop access to further hydrogen sulphide molecules.

When reaction was complete and the excess of oxygen had been pumped off, heating the sorbent caused the more strongly sorbed sulphur-containing gases to be desorbed. It is postulated that as the temperature is increased the sulphur monoxide molecules become mobile, and in the absence of oxygen would be likely to react together to form sulphur dioxide and sulphur, $2SO \longrightarrow SO_2 + S$. The sulphur dioxide would be desorbed and the sulphur would remain in the channels of the zeolite. Conditions of low mobility appear to be temperatures of $<100°$ for the calcium form of sieve 13X and 0° or less for sieve 4A. This difference in behaviour can be attributed to the greater force of attraction between sorbent and sorbed molecules when the interstitial ions are bivalent rather than univalent.

Replacement of sodium ions by calcium ions without change in the aluminosilicate framework or in experimental conditions leads to a decrease in the v_{O_2}/v_{H_2S} ratio and this has been demonstrated by a change from sieve 4A to sieve 5A and from the sodium to the calcium form of sieve 13X. A change of univalent cation, *e.g.*, of sodium for potassium, had little effect.

Under conditions where adsorbed sulphur monoxide is mobile, reaction can proceed by

[6] Lewis, *J. Phys. Chem.*, 1959, **63**, 527.
[7] Barrer, *Ann. Reports*, 1944, **41**, 31.

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collision with another molecule of the same species or with a molecule of oxygen to form sulphur trioxide. When the original hydrogen sulphide concentration and hence the sulphur monoxide concentration is low, reaction to form sulphur trioxide should be more likely. The results in Table 1 show that the higher the initial concentration of hydrogen sulphide, the lower is the final v_{O_2}/v_{H_2S} ratio.

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(W. E. A.) The University, Nottingham. [*Received, June 5th,* 1961.]

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937. *The Cumulative Effect of Substituents in an Aromatic Nucleus on Reactions of the Side-chain: The Effect of Chlorine as Substituent on the Reaction of Benzoyl Chlorides with Aniline, on the Alkaline Hydrolysis of Ethyl Benzoates, and on the Ionisation of Benzoic Acids.*

By J. G. Mather and J. Shorter.

Rate coefficients (usually at four temperatures) have been measured for the reactions of benzoyl chloride, three monochlorobenzoyl chlorides, and six dichlorobenzoyl chlorides with aniline in benzene, and for the alkaline hydrolysis of ethyl benzoate, three ethyl monochlorobenzoates, and all ethyl dichlorobenzoates except the 2,6-isomer, in aqueous ethanol containing 84·6% (w/w) of ethanol. Arrhenius parameters have been evaluated. Values of pK_a in water at 22° have been measured potentiometrically for all dichlorobenzoic acids, except the 3,4-isomer.

The relative effect of *m*-Cl and *p*-Cl on the reactivity of benzoyl chloride towards aniline is compared with their relative effect on alkaline ester hydrolysis and on acid dissociation. *o*-Chlorobenzoyl chloride is the most reactive of the three isomers, and there is no distinctive effect of *o*-Cl on the Arrhenius non-exponential factor (cf. alkaline ester hydrolysis), but a second *o*-Cl reduces the reactivity greatly. The relation between the effects of *o*-Cl, *m*-Cl, and *p*-Cl on reactivity in the benzoylation is examined in terms of a simple electrostatic theory.

The 3,5-, 2,4-, and 2,5-dichloro-compounds show strict additivity of substituent effects in ester hydrolysis and acid dissociation, but departures from additivity in the reaction of benzoyl chlorides with aniline are considerable. In the case of 3,4-dichloro-compounds there is a departure from strict additivity of substituent effects which is probably due to electrostatic interaction of the C–Cl dipoles. The 2,3-dichloro-compounds show an additional effect due to the three substituents' being adjacent on the ring. The ionisation of 2,6-dichlorobenzoic acid shows strict additivity, whereas in the other systems the 2,6-isomers show great departures.

During recent years attention has been paid to the combined effect of two or more nuclear substituents on the reactivity of aromatic side-chains, in order to discover the extent to which substituent effects are additive and to explain departures from strict additivity. Considerable variety and complexity of behaviour has been observed.[1-5] We felt that it would be valuable to study systematically the effect of a particular substituent in various types of reaction. The small monatomic substituent chlorine was chosen since it produces large changes in the reactivity of aromatic compounds. The reactions selected

[1] (*a*) Stubbs and Hinshelwood, *J.*, 1949, S71; (*b*) Bose and Hinshelwood, *J.*, 1958, 4085.
[2] (*a*) Jones and Robinson, *J.*, 1955, 3845; (*b*) Crocker and Jones, *J.*, 1959, 1808; (*c*) Jones and Watkinson, *J.*, 1958, 4064.
[3] Shorter and Stubbs, *J.*, 1949, 1180.
[4] Peltier, *Bull. Soc. chim. France*, 1958, 994, and papers referred to therein.
[5] Dippy, Hughes, and Bray, *J.*, 1959, 1717, and papers referred to therein.

were that between substituted benzoyl chlorides and aniline, the alkaline hydrolysis of substituted ethyl benzoates, and the ionisation of substituted benzoic acids.

The kinetics of the reaction between benzoyl chloride and aniline in benzene solution were first studied by Hinshelwood and his colleagues.[6] The reaction takes place quantitatively according to the equations:

$$Ph{\cdot}COCl + NH_2Ph = Ph{\cdot}NH{\cdot}COPh + HCl$$
$$PhNH_2 + HCl = Ph{\cdot}NH_2{}^+Cl^-$$

the aniline hydrochloride being precipitated. The reaction is of the second order, the first stage being slow and the second very rapid. The second-order rate coefficients fall slightly with decrease in the initial concentration of the reactants. (In certain solvents such as hexane and carbon tetrachloride the kinetic behaviour is complicated,[6a] and the dilution effect in benzene is presumably a residuum of such complication.) In the early work the effect of *meta*- and *para*-substituents in the benzoyl chloride and aniline molecules was investigated. Stubbs and Hinshelwood [1a] studied the effect of *ortho*-substituents in the aniline molecule and also the cumulative effect of substituents in the aniline molecule. More recently Benkeser *et al.*[7] have studied the reactions of several *meta*- and *para*-substituted benzoyl chlorides with aniline in benzene; Bose and Hinshelwood [1a] have investigated the reaction in nitrobenzene and other polar solvents; Elliott and Mason [8] have examined kinetic isotope effects; and various aspects of the benzoylation of aniline have been investigated by Litvinenko and his colleagues.[9]

There have been many studies of the influence of nuclear substituents on the rate of alkaline hydrolysis of ethyl benzoate and the ionisation of benzoic acid, so only those concerned with the cumulative effect of two or more substituents will be mentioned here.

Blakey, McCombie, and Scarborough [10] measured the rates of hydrolysis of mono- and di-substituted ethyl benzoates in aqueous ethanol, including all ethyl dichlorobenzoates except the 2,6-isomer. For ethyl *o*-chlorobenzoate, however, they obtained two sets of rate coefficients differing by some 30% under the same experimental conditions; they were unable to explain this. Studies of the combined effect of two substituents *ortho* to each other on the saponification of ethyl benzoate have been made by Price and Lincoln, and by Westheimer and Metcalf in order to investigate steric inhibition of resonance.[11] Brynmor Jones and Robinson [2a] studied a variety of 3,4- and 3,5-disubstituted ethyl benzoates, including the dichloro-esters. The 3,5-compounds showed good additivity of substituent effects, but the 3,4-compounds showed appreciable departures from strictly additive behaviour.

Ten years ago few really accurate measurements of the dissociation constants of disubstituted benzoic acids had been made, although there was much accurate information on the dissociation constants of monosubstituted acids.[12] In 1949 Shorter and Stubbs [3] surveyed the available data for the classical dissociation constants of disubstituted benzoic acids. The change in the free energy of ionisation caused by two or more substituents in benzoic acid was shown in a number of cases to be very nearly the algebraic sum of the effects of the individual groups, but certain 2,3- and 2,6-disubstituted acids provided striking exceptions. In the last 10 years a number of accurate measurements of the dissociation constants of disubstituted benzoic acids have been made, mainly by Dippy [5] and by Peltier [4] and their colleagues. Considerable variety of behaviour in the cumulative effects of substituents has been observed. When the present work was started no value for the

[6] (*a*) Grant and Hinshelwood, *J.*, 1933, 1351; (*b*) Williams and Hinshelwood, *J.*, 1934, 1079; (*c*) Newling, Staveley, and Hinshelwood, *Trans. Faraday Soc.*, 1934, **30**, 597.
[7] Benkeser, de Boer, Robinson, and Sauve, *J. Amer. Chem. Soc.*, 1956, **78**, 682.
[8] Elliott and Mason, *Chem. and Ind.*, 1959, 488.
[9] See, *e.g.*, Litvinenko and Aleksandrova, *Ukrain. khim. Zhur.*, 1960, **26**, 66.
[10] Blakey, McCombie, and Scarborough, *J.*, 1926, 2863.
[11] Price and Lincoln, *J. Amer. Chem. Soc.*, 1951, **73**, 5838; Westheimer and Metcalf, *J. Amer. Chem. Soc.*, 1941, **63**, 1339.
[12] Dippy, *Chem. Rev.*, 1939, **25**, 151.

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dissociation constants of any dichlorobenzoic acids had been published. Davis and Hetzer [13] have recently presented values for 2,4-, 3,4-, and 2,6-dichlorobenzoic acid, measured by potentiometric titration or spectrophotometry, and Dippy, Hughes, and Bray [5] have studied 2,4-, 2,5-, and 2,6-dichlorobenzoic acid by conductivity measurements.

Experimental

Preparation and Purification of Benzoic Acids.—Commercial benzoic acid, the monochlorobenzoic acids, and 2,4-, 2,5-, and 3,4-dichlorobenzoic acid were crystallised to constant m. p. from aqueous ethanol, glacial acetic acid, and benzene. Ethyl esters made from these acids gave satisfactory second-order kinetics in alkaline hydrolysis.

2,3-Dichlorobenzoic acid was prepared from 2,3-dichloroaniline by diazotisation and a Sandmeyer reaction, followed by acid hydrolysis of 2,3-dichlorobenzonitrile. To obtain pure 2,3-dichlorobenzoic acid it was essential to purify 2,3-dichloroaniline carefully by fractional freezing, and to isolate the nitrile by steam-distillation and crystallise it from ethanol. The nitrile was hydrolysed by refluxing with 60% sulphuric acid for 1 hr. 2,3-Dichlorobenzoic acid was crystallised to constant m. p. from aqueous ethanol.

2,6-Dichlorobenzoic acid was prepared from 2,6-dichlorotoluene by Lehmstedt and Schrader's method.[14]

3,5-Dichlorobenzoic acid was prepared from anthranilic acid as described by Brynmor Jones and Robinson.[2g]

Preparation and Purification of Benzoyl Chlorides and Aniline.—The benzoyl chlorides were usually made from the pure benzoic acids by treatment with thionyl chloride, and were repeatedly distilled under reduced pressure. In certain cases carefully fractionated commercial samples of the benzoyl chlorides were used. Aniline was purified by distillation at atmospheric and finally under reduced pressure.

Preparation and Purification of Ethyl Benzoates.—The benzoic acids were usually esterified with ethanol and sulphuric acid. Liquid esters were fractionated under reduced pressure; solid esters were recrystallised from light petroleum (b. p. $<30°$). In each case the ester was purified until it gave consistent second-order kinetics in alkaline hydrolysis. It was necessary to redistil certain esters every few days to keep them in a condition to satisfy this kinetic criterion of purity.

In the case of ethyl 2,3-dichlorobenzoate it was found that the product of esterification by the action of ethyl iodide on the silver salt gave more consistent kinetics than that made by the usual method. Ethyl 2,6-dichlorobenzoate was made by the silver salt–ethyl iodide method.

Purification of Solvents.—" AnalaR " benzene was dried ($MgSO_4$) and fractionated through a Widmer column (b. p. 79·5—80°, lit., 80·1°; n_D^{20} 1·5007, lit., 1·5009). Williams and Hinshelwood [6b] showed that elaborate purification of benzene was unnecessary.

Ethanol was purified by the magnesium–iodine method. It was mixed with boiled-out conductivity water to give a mixture containing 84·6% (w/w) of ethanol.

Measurement of Rate Coefficients for the Benzoylation Reaction.—As in earlier work the reaction was followed by filtering-off the aniline hydrochloride produced, dissolving this in water, and estimating the chloride by Volhard's method.[1,6] Since there is a slight effect of dilution on the rate coefficients it was desirable for comparison of coefficients to be made at standard concentrations. The reaction between aniline and the chloro-substituted benzoyl chlorides being rapid, low concentrations of reactants were used: 0·005M-aniline and 0·0025M-benzoyl chloride. This is Williams and Hinshelwood's " Dilution III." [6b] If the initial concentration of benzoyl chloride is a and that of aniline $2a$ mole $l.^{-1}$, and x is the percentage change after t min., then $k = x/120a.t(100 - x)$, where k is the second-order rate coefficient in l. mole^{-1} sec.$^{-1}$. At temperatures other than 15° or 25°, rate coefficients were corrected for thermal expansion or contraction of the solvent.

Typical results are shown in Table 1. The mean deviation in k in most experiments was 1—2% over 80% of the course of the reaction.

Measurement of Rate Coefficients in Ester Hydrolysis.—Equal concentrations (0·05M) of ester and sodium hydroxide (carbonate-free) were used. The reaction was followed by running

[13] Davis and Hetzer, *J. Phys. Chem.*, 1957, **61**, 123.
[14] Lehmstedt and Schrader, *Ber.*, 1937, **70**, 1526.

TABLE 1.

Aniline and 2,4-dichlorobenzoyl chloride at 15°.

t (min.)	5	10	15	25	40	60
x (%)	30·75	46·9	57·1	68·25	78·05	83·8
10^3k (l. mole^{-1} sec.$^{-1}$)	29·55	29·50	29·68	28·81	29·60	28·77

Mean value of $10^3k = 29·32$ (±1·2%).

Aniline and benzoyl chloride at 25°.

t (min.)	10	20	40	60	80	100	140	200
x (%)	16·6	28·75	45·4	55·4	61·9	66·5	74·1	80·5
10^3k (l. mole^{-1} sec.$^{-1}$)	6·67	6·71	6·92	6·91	6·77	6·63	6·81	6·91

Mean value of $10^3k = 6·79$ (±1·5%).

samples into ice-cold hydrochloric acid (measured excess) and titrating the excess of acid with standard sodium hydroxide solution (bromothymol Blue as indicator).[20,15] The reaction was timed from the removal of the first sample and the analysis of this provided the initial concentration a for the second-order rate expression: $k = x/60a.t(a - x)$, where x is the concentration of ester or alkali (mole l.$^{-1}$) that has reacted after time t (min.), k being in units l. mole^{-1} sec.$^{-1}$.

Typical results are shown in Table 2. The mean deviation in k in most experiments was 1—2% over about 70% of the course of the reaction.

Measurement of Strengths of Benzoic Acids by Potentiometric Titration.—A direct-reading pH-meter (Electronic Instruments Ltd., model 23A) was used. The titration vessel was fitted with glass electrode, calomel reference electrode (saturated potassium chloride), and mechanical stirrer; a potassium hydrogen phthalate buffer solution was used for standardisation. Solutions

TABLE 2.

Alkaline hydrolysis of ethyl 2,4-dichlorobenzoate at 25°.

t (min.)	0	15	30	45	60	80	100	120	150
10^3x (mole l.$^{-1}$)	0·0	9·9	16·5	20·4	23·5	26·7	28·8	30·8	32·6
10^3k (l. mole^{-1} sec.$^{-1}$)	—	7·33	7·57	7·26	7·25	7·30	7·15	7·36	7·22

$a = 0·0440$ mole l.$^{-1}$. Mean value of $10^3k = 7·31$ (±1·2%).

Alkaline hydrolysis of ethyl 2,3-dichlorobenzoate at 15°.

t (min.)	0	10	20	40	80	130	220	300	360
10^3x (mole l.$^{-1}$)	0·0	2·6	5·1	8·9	15·4	20·9	26·9	30·3	32·0
10^3k (l. mole^{-1} sec.$^{-1}$)	—	2·02	2·10	2·01	2·09	2·11	2·07	2·05	2·00

$a = 0·0476$ mole l.$^{-1}$. Mean value of $10^3k = 2·06$ (±1·8%).

of the benzoic acids (0·01, 0·001, or 0·0005M according to solubility) were made up in boiled-out conductivity water under nitrogen. 50 ml. portions were titrated with carbonate-free sodium hydroxide (0·04N for 0·01M-acid; 0·01N for 0·001 or 0·0005M-acid), the pH being read after each addition of 0·25 ml. of alkali. The titration was continued to the theoretical half-equivalence point. Strict temperature control was not necessary since pK_a varies only slightly with temperature; the experiments were made at 22° ± 0·5°. Values of pK_a were calculated by means of the following equations: [13]

$$pK_a = pH - \log([B^-]/[HB]) - \log f_{B^-}$$

$$-\log f_{B^-} = 0·5\sqrt{\mu}/(1 + 1·32\sqrt{\mu}),$$

where $[B^-]$ is the concentration of benzoate ion, [HB] is that of undissociated benzoic acid, and f_{B^-} is the activity coefficient of the benzoate ion at ionic strength μ. Table 3 shows a typical set of values of pK_a at different points in the titration. The mean deviation in such sets of values of pK_a was usually 0·01—0·02.

With a 0·01M-solution of benzoic acid itself pK_a was found to be 4·21, in good agreement with the value of 4·203 given by Dippy [12] (conductivity measurements, 25°) and that of 4·205 obtained by Jones and Parton [16] (E.M.F. measurements, 20°). At 0·001M-concentration,

[15] Evans, Gordon, and Watson, *J.*, 1937, 1430.
[16] Jones and Parton, *Trans. Faraday Soc.*, 1952, **48**, 8.

TABLE 3.

Determination of pK_a for 2,5-dichlorobenzoic acid at 22°.

NaOH (ml.)	0·25	0·50	0·75	1·00	1·25	1·50	1·75	2·00
pH	3·16	3·18	3·21	3·24	3·27	3·30	3·34	3·38
pK_a	2·65	2·62	2·63	2·66	2·63	2·62	2·64	2·65

50 ml. of 0·001M-acid were titrated with 0·01N-sodium hydroxide. Mean value of $pK_a = 2·64 \pm 0·01$.

however, the observed value was 4·30 and at 0·0005M it was 4·32. We attribute this apparent rise in pK_a with dilution to the failure of the saturated potassium chloride bridge to eliminate completely the liquid-junction potential at very low concentrations of organic acid and salt. We therefore express the results for the chloro-substituted acids as ΔpK_a values, *i.e.*, relative to benzoic acid under the same conditions of concentration. Thus the ΔpK_a value for 2,5-dichlorobenzoic acid, calculated from the results in Table 3, is 4·30 − 2·64 = 1·66.

DISCUSSION

Influence of Chlorine Substituents in Benzoyl Chloride on Reactivity towards Aniline.—Rate coefficients, k, activation energies, E, and non-exponential factors, A, from the Arrhenius equation are shown in Table 4.

Williams and Hinshelwood [6b] showed that electron-attracting substituents in the benzoyl chloride molecule increase the reactivity towards aniline. Withdrawal of electrons from the carbonyl chloride group facilitates the approach of the lone pair of electrons of the amino-group to the carbonyl carbon atom and the attainment of the transition state, which may be represented [8] as in Fig. 1. It is therefore to be expected that *m*- and *p*-chlorobenzoyl chloride will be more reactive than benzoyl chloride. In fact all three mono-

TABLE 4.

Rate coefficients and Arrhenius parameters for reaction of benzoyl chlorides with aniline.

Subst.	10^3k (l. mole^{-1} sec.$^{-1}$) 5°	15°	25°	35°	E (cal. mole^{-1})	log A
H	3·33	5·07	6·79 [a]	11·8	6910	3·95
o-Cl	15·6	22·0	30·4	42·2	5610	3·60
m-Cl	9·29	14·3	19·7	27·9	6140	3·81
p-Cl	4·91 [b]	7·56	10·7 [c]	15·8	6540 [d]	3·83
2,3-Cl_2	22·2	31·4	42·9	60·5	5630	3·77
2,4-Cl_2	19·7	29·3	41·3	57·7	6070	4·07
2,5-Cl_2	32·9	47·0	66·3	88·7	5630	3·95
2,6-Cl_2	0·110 *	0·153 †	0·0152	—	10,630	3·99
3,4-Cl_2	11·7	16·6	25·3	32·3	5890	3·70
3,5-Cl_2	23·3	32·6	43·7	58·7	5200	3·46

* At 60°. † At 70°.

Values of k are accurate within ±2%. Values of E are accurate within ±300 cal. mole^{-1}. Values of log A are accurate to within ±0·3. Values given by Williams and Hinshelwood [6b] are *a* 6·88; *b* 4·65; *c* 10·4; *d* 7000.

chlorobenzoyl chlorides are more reactive than benzoyl chloride; values of E are lower and those of k higher for the chloro-substituted compounds. *m*-Chlorobenzoyl chloride is more reactive than the *para*-isomer; in the latter the $-I$ effect of chlorine is in competition with its $+M$ effect. If the effect of a substituent upon reactivity is expressed as log (k/k_0), where k refers to the substituted compound and k_0 to the unsubstituted compound, then the relative effect of *m*-Cl and *p*-Cl upon reactivity is 2·6 (mean value for the four temperatures in Table 4). In the saponification of ethyl benzoates the corresponding value is 1·4, derived from the five temperatures in Table 5. The ratio of the Hammett σ values for *m*-Cl and *p*-Cl is 1·65, this being essentially the relative effect of

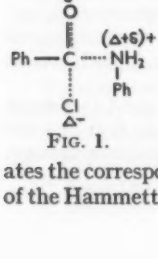

FIG. 1.

the substituents on the dissociation of benzoic acid.[17] This striking difference between the effect of chlorine substituents in the benzoylation on the one hand and in ester saponification and acid dissociation on the other may possibly be explained along the following lines. In the transition state for ester hydrolysis the seat of the reaction carries a negative charge, as does the final state in the acid dissociation, the benzoate ion. It may be that under these circumstances the $+M$ mesomeric effect of *p*-Cl has less influence than in the transition state for the benzoylation of aniline, where the seat of the reaction carries no resultant charge. Since the $+M$ effect reduces reactivity in all three reactions under consideration, the relative effect of *m*-Cl and *p*-Cl on reactivity should be lower in ester saponification and acid dissociation than in the benzoylation, as found experimentally.

The relative effect of *m*-Br and *p*-Br in benzoyl chloride calculated from the results of Benkeser *et al.*[7] is 2·01; the ratio of the σ values is 1·68. The behaviour of bromine is thus qualitatively similar to that of chlorine but not so striking. The greater $+M$ effects of certain *para*-substituents in benzoylation than in the dissociation of benzoic acid can also be seen from the *effective* σ values calculated by van Bekkum, Verkade, and Wepster [18] for substituents in the benzoyl chloride molecule.[7] These σ values are: *p*-Cl, +0·172; *p*-Br, +0·202; *p*-Me, −0·231; *p*-OMe, −0·499. The σ values, based on the results of Dippy and his colleagues for the dissociation of substituted benzoic acids,[12] are *p*-Cl, +0·224; *p*-Br, +0·232; *p*-Me, −0·170; *p*-OMe, −0·268. Values in the former set are more negative than corresponding values in the latter, corresponding to a greater $+M$ effect.

The relative effect of *m*-Cl and *p*-Cl on the reactivity of aniline is 1·8, calculated from Stubbs and Hinshelwood's results.[1a] (Electron-attracting substituents in the aniline molecule reduce reactivity.) This value is appreciably smaller than that for substituents in benzoyl chloride. In *p*-chloroaniline the operation of the $+M$ effect of chlorine will enhance reactivity, but the mesomeric effect acts in opposition to the $+M$ effect of the amino-group and may therefore be of less influence than in *p*-chlorobenzoyl chloride. This would lead to a lower value for the relative effect of *m*-Cl and *p*-Cl on the reactivity of aniline than for their relative effect in benzoyl chloride.

o-Chlorobenzoyl chloride is the most reactive of the three isomers. In this behaviour the benzoylation is in marked contrast to the alkaline hydrolysis of ethyl benzoates, where the *o*-chloro-compound is the least reactive of the three isomers; ethyl *o*-chlorobenzoate has the lowest activation energy but the non-exponential factor is much lower than those of the *meta*- and the *para*-isomer (Table 5). *o*-Chlorobenzoyl chloride has the lowest activation energy of the isomers but the non-exponential factors of all three isomers are approximately the same (Table 4). The values of log A for *m*-chloro-, *p*-chloro-, 3,4-dichloro-, and 3,5-dichloro-benzoyl chloride and for benzoyl chloride itself have a mean value of $3{\cdot}8 \pm 0{\cdot}1$. The values for *o*-chloro- and 2,3-, 2,4-, 2,5-, and 2,6-dichloro-benzoyl chloride have a mean value of $3{\cdot}9 \pm 0{\cdot}2$. The absence of an effect of *o*-Cl on log A is particularly striking in the case of 2,6-dichlorobenzoyl chloride; the second *o*-chlorine atom greatly *reduces* the reactivity but this is due entirely to an increase in the activation energy. Stubbs and Hinshelwood [1a] found that there was no effect on log A of *ortho*-substituents in aniline, the groups studied being *o*-Me, 2,6-Me_2, *o*-Cl, and *o*-NO_2. The constancy of log A for a variety of *ortho*-substituents in aniline and for *o*-Cl and 2,6-Cl_2 at least in benzoyl chloride is of interest in connection with the transition state, which is now to be discussed.

The Transition State in the Reaction between Benzoyl Chloride and Aniline.—A representation of the transition state due to Elliott and Mason [8] has been shown above. A model of the transition state can usefully be made from molecular models of the Stuart pattern. The carbon and nitrogen atoms at the reaction centre are represented by a " paraffinic carbon " and a " quaternary nitrogen," respectively. We may distinguish two possible

[17] Jaffé, *Chem. Rev.*, 1953, **53**, 191.
[18] van Bekkum, Verkade, and Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.

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extreme configurations for the transition state. In one form, which we shall call the extended configuration, the rings are on opposite sides of the C–N bond linking the two reacting molecules, and in the most symmetrical arrangement the rings lie parallel (Fig. 2a). There is fair freedom of rotation about the ring–COCl bond, but rotation about the ring–NH bond is greatly restricted; when the ring of the aniline is rotated the *ortho*-hydrogen atoms engage with the oxygen and chlorine atoms. In the other form, which we shall call the compact configuration, the rings are on the same side of the C–N bond linking the two reacting molecules. The rings are inclined at an angle to each other (Fig. 2b). There is little freedom of rotation for either ring; slight rotation of either ring causes it to engage with the other.

It seems likely that the withdrawal of the hydrogen and the chloride ions would occur more easily from the compact than from the extended configuration. In the compact configuration, however, the rings are pressed rather close together, since the C–N partial bond is not likely to be more than 2 Å long. The normal closest distance of lateral approach of two aromatic rings,[19] as for example in the formation of charge-transfer complexes,[20] is 3·2—3·5 Å. Thus the compact configuration would involve very considerable interaction of the π-electron systems of the two rings, and this would make it energetically very

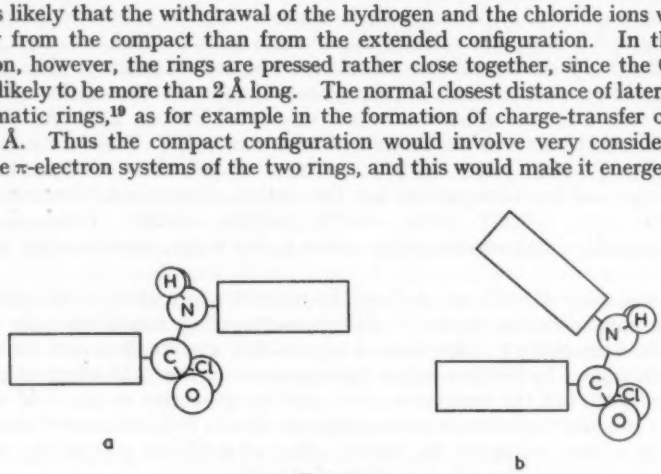

FIG. 2.

unfavourable compared with the extended configuration. We therefore conclude that the actual transition state will approximate more closely to the extended than to the compact configuration.

Study of the model shows that a chlorine atom, a methyl group, or a nitro-group can be introduced into either *ortho*-position of the aniline in the extended configuration of the transition state without steric strain and without much increase in the restriction of the rotation of the aniline ring, the rotation of which is already greatly restricted. The absence of any effect on log A for *ortho*-substituents in the aniline molecule is thus readily explicable.

We pass now to the effect of introducing an *o*-chlorine atom into the benzoyl chloride molecule. Inspection of the model suggests that this should restrict greatly the rotation of the benzoyl chloride ring in the transition state (as compared with the initial state). If this were really so, however, a fall in log A would result, as in ester hydrolysis. The constancy of the non-exponential term means that the rotation of the ring in the transition state for benzoyl chloride itself must be much more restricted than would at first sight be supposed. We suggest that, in the transition state for benzoyl chloride reacting with aniline, the two rings lie parallel, with little freedom of rotation for either ring. The model shows that in this arrangement an *o*-chlorine atom in the benzoyl chloride molecule can be accommodated adjacent to the oxygen atom without much steric strain or twisting of the ring. There is little decrease in the freedom of rotation, because this is supposed already

[19] Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, New York, 1940, 2nd edn., p. 172.
[20] Andrews, *Chem. Rev.*, 1954, **54**, 765.

restricted in the transition state for benzoyl chloride itself. On the other hand an *o*-chlorine atom can only lie adjacent to the bulky reacting chlorine atom with considerable steric strain. When two *o*-chlorine atoms are present the transition state can thus only be achieved with much steric strain or stretching of bonds. We have, therefore, a ready explanation of the observation that, while the first *o*-chlorine atom in benzoyl chloride enhances reactivity, the second reduces it, raising the activation energy by some 5000 cal. mole^{-1}.

The preference of the transition state for the extended configuration with the rings parallel may possibly be due to interaction with the solvent. The transition state is more polar than the initial state of the reactants [18,8] and will therefore be more highly solvated. Orientation of the benzene molecules around the transition state might well be favoured by parallelism of the benzoyl chloride and aniline rings.

The Relation between the Effects of o-, m-, *and* p-*Chlorine Atoms on Reactivity in the Benzoylation of Aniline.*—For a number of side-chain reactions in the aromatic series it is possible to correlate the effect of a *meta*-substituent on reactivity and the dipole moment associated with the substituent when attached to the aromatic ring, which is a measure of the strength of the electric field produced by the substituent at the seat of the reaction.[21] The correlation is less good in the case of *para*-substituents owing to the intervention of the mesomeric effect. With *ortho*-substituents there is usually little point in attempting such a correlation, since the operation of steric effects will be superimposed on the influence of the electric field of the substituent. Steric effects of *ortho*-substituents seem relatively unimportant in the benzoylation of aniline in benzene, as judged by the constancy of the non-exponential factor, and an attempt to correlate reactivity and the dipole moments of *ortho*-substituents is profitable. Stubbs and Hinshlewood [18] showed that there was a relation between free energy of activation and dipole moment for *ortho*-substituted anilines. Sufficient *ortho*-substituted benzoyl chlorides have not yet been studied, but an attempt to understand the relative effect of *o*-Cl and *p*-Cl in electrostatic terms is worthwhile.

Jenkins [22] sought to relate the strength of a substituted benzoic acid to the electric field produced by the substituent at the carbon atom to which the carboxyl group is attached. He calculated the electrostatic potentials due to various substituents in the *ortho*-, *meta*-, and *para*-positions, assuming that each substituent could be regarded as having a small dipole, of moment equal to the observed bond moment, located half-way between the carbon atom of the ring and the first substituent atom. The electrostatic potential *in vacuo* at a certain point due to a small dipole whose centre is r cm. away and whose axis is inclined at an angle θ to the line of length r is $\psi = -\mu \cos\theta/r^2$, where μ is the dipole moment. The values of ψ are: *o*-Cl, +0·355; *m*-Cl, +0·158; and *p*-Cl, +0·130.

We now assume that chlorine substituents affect the reactivity of benzoyl chloride through changing the electrostatic potential at the carbon atom to which the COCl group is attached. This is equivalent to the assumption made by Jenkins for benzoic acid, and amounts to regarding the C·COCl system " as a more or less perfect conductor or equipotential surface." The effects of chlorine substituents on reactivity expressed as log (k/k_0) should then be in the ratio of the electrostatic potentials given above. The relative effect of *o*-Cl and *p*-Cl has the mean value 3·8 for the four temperatures in Table 4, compared with a value of 2·73 for the ratio of the electrostatic potentials. It is satisfactory that these quantities agree approximately. One should be cautious in trying to explain the difference between them. The assumption at the beginning of this paragraph may not be strictly valid. Further we have used electrostatic potentials calculated for a vacuum. This does not matter in assessing the relative effect of *o*-Cl and *p*-Cl provided that the effective dielectric constant is the same for both positions, but this could well not be the case. However, it is worth noting that the reactivity ratio is higher than that of the electrostatic potentials and this could mean that the mesomeric effect of the chlorine

[21] Watson, " Modern Theories of Organic Chemistry," Oxford, 1941, 2nd edn., p. 56.
[22] Jenkins, *J.*, 1939, 640; see also *J.*, 1939, 1137, 1780.

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atom is transmitted less effectively from an *ortho*-position than from a *para*-position. The mean relative effect of *m*-Cl and *p*-Cl on the reactivity of benzoyl chloride is 2·6, as noted above, where it was suggested that this indicated a rather powerful operation of the mesomeric effect of *p*-Cl. In this connection it is interesting that the ratio of the electrostatic potentials is much lower, 1·22; this confirms the operation of a powerful mesomeric effect of *p*-Cl reducing reactivity.

We may discuss the effect of chlorine substituents on the reactivity of aniline in the same way, assuming that the electrostatic potential at the carbon atom to which the amino-group is attached governs the reactivity. The relative effect of *o*-Cl and *p*-Cl on reactivity is 3·2 (Stubbs and Hinshelwood's results [1a]). The ratio of the electrostatic potentials is lower, 2·73, but the agreement is better than for the corresponding benzoyl chlorides. As before, it may be that the mesomeric effect of the chlorine atom is transmitted less effectively from an *ortho*- than from a *para*-position. In aniline the mesomeric effect of chlorine as a substituent seems to be of less influence than in benzoyl chloride (see above), and it is thus reasonable that the agreement between reactivity and electrostatic potentials should be better in aniline than in benzoyl chloride. In accordance with this the relative effect of *m*-Cl and *p*-Cl on the reactivity of aniline is 1·8, compared with 1·22 for the ratio of the electrostatic potentials, and 2·6 for the relative effect of *m*-Cl and *p*-Cl on the reactivity of benzoyl chloride.

The Alkaline Hydrolysis of Chloro-substituted Ethyl Benzoates in 84·6% *Ethanol.*—Rate coefficients, k, activation energies, E, and non-exponential factors, A, from the Arrhenius equation are shown in Table 5. No appreciable hydrolysis of ethyl 2,6-dichlorobenzoate could be detected even after some days at the reflux temperature of the solvent.[23]

Earlier work on the influence of a single chloro-substituent on the alkaline hydrolysis of ethyl benzoate showed that log A was unaffected by *m*- or *p*-Cl,[15,24] but was appreciably diminished by *o*-Cl.[15] The results in Table 5 show that the same effects are found with

TABLE 5.

Rate coefficients and Arrhenius parameters for alkaline hydrolysis of ethyl benzoates in 84·6% ethanol.

	10^3k (l. mole^{-1} sec.$^{-1}$)					E	
Subst.	5°	15°	25°	35°	45°	(cal. mole^{-1})	log A
H	0·082	0·242	0·646	1·82	4·48	17,610[f]	9·75
o-Cl	—	0·568	1·42[a]	3·42	7·98	16,020[g]	8·91
m-Cl	0·641	1·86	4·79[b]	13·1	30·3	16,990[h]	10·16
p-Cl	0·330	1·16	2·80[c]	7·40	17·6	17,250[i]	10·12
2,3-Cl$_2$	—	2·06	5·07	11·4	24·8	15,070	8·75
2,4-Cl$_2$	—	2·96	7·29	15·7	32·6	14,500	8·49
2,5-Cl$_2$	—	5·36	11·0	27·0	59·1	14,720	8·88
3,4-Cl$_2$	2·34	6·42	15·7[d]	37·2	—	15,620	9·66
3,5-Cl$_2$	5·59	16·4	36·1[e]	92·9	—	15,690	10·10

Values of k are accurate to within ±2%. Values of E are accurate to within ±300 cal. mole^{-1}. Values of log A are accurate to within ±0·3.

To eliminate the effect of small differences in solvent composition and experimental conditions comparison of values for k with data from earlier work is best made in terms of $k/k_0 = r$, the ratio of coefficients for substituted and unsubstituted ethyl benzoates.

[a] $r = 2·20$; Evans, Gordon, and Watson (*J.*, 1937, 1430) give $r = 2·24$ for 84·8% ethanol. [b] $r = 7·42$; Evans, Gordon, and Watson give 7·68; Brynmor Jones and Robinson (*J.*, 1955, 3845) give $r = 7·62$ for 84·6% ethanol. [c] $r = 4·33$; Brynmor Jones and Robinson give 4·34; Ingold and Nathan (*J.*, 1936, 222) give $r = 4·31$ for 85·0% ethanol. [d] $r = 24·3$; Brynmor Jones and Robinson give 24·1. [e] $r = 55·8$; Brynmor Jones and Robinson give 65·3. [f] Evans, Gordon, and Watson; Ingold and Nathan; and Brynmor Jones and Robinson give 17,700. [g] Evans, Gordon, and Watson give 15,700. [h] Evans, Gordon, and Watson give 16,400. [i] Ingold and Nathan give 16,800.

the ethyl dichlorobenzoates. The non-exponential factors for ethyl 3,4- and 3,5-dichlorobenzoate are close to those of ethyl *m*- and *p*-chlorobenzoate and of ethyl benzoate, the

[23] See summary and references in Dippy, Evans, Gordon, Lewis, and Watson, *J.*, 1937, 1421.
[24] Ingold and Nathan, *J.*, 1936, 222.

average value of log A for the five compounds being 10·0 ± 0·2. The non-exponential factors for ethyl 2,3-, 2,4-, and 2,5-dichlorobenzoates lie close to that for ethyl *o*-chlorobenzoate. The average value of log A for the four compounds is 8·8 ± 0·1. The lowering of log A by *o*-Cl was formerly ascribed to chelation in the transition state between the carbonyl-oxygen atom of the ester group and the *ortho*-substituent.[15] More recently, following Kadesch,[25] it has been related to the steric effect of the substituent twisting the ester group with respect to the benzene ring, and hindering access of the hydroxyl ion on one side of the ester group.[26]

The value of E for ethyl *o*-chlorobenzoate is *lower* than that of the *para*-isomer by about 1200 cal. mole.$^{-1}$. Earlier values of the activation energies differ by about the same amount, 1100 cal. mole^{-1} (Table 5 footnotes), and Evans, Gordon, and Watson [15] drew attention to this. In the saponification of ethyl benzoates in 56% acetone the activation energies of these compounds are related in the same way.[27] The transfer of the chlorine atom from the *para*- to an *ortho*-position may conceivably change the activation energy through changing various factors, *e.g.*, the transmission of the electron-attracting effect of the chlorine to the reaction centre, the mesomeric interaction of benzene ring and ester side-chain, and the solvation of ester and transition state. It is impossible as yet to assess what part is played by these.

Assessment of the Cumulative Effect of Substituents.—The alkaline hydrolysis of ethyl benzoates. Experimentally measured values of the activation energy are not accurate enough for assessing the cumulative effect of substituents; free energies of activation are therefore used.[1a] The Arrhenius non-exponential factor, however, is unaffected (within the limits of experimental error) by *m*- or *p*-Cl and changes in free energy of activation thus reflect changes in activation energy. For each substituted ethyl benzoate not containing *o*-Cl the quantity $\Delta E'$ (obs.) = 2·303 RT log (k/k_0) has been evaluated at the various temperatures used for rate measurements; k is the observed rate coefficient for the substituted ethyl benzoate, and k_0 is that for ethyl benzoate itself, derived from the Arrhenius equation with E = 17,610 cal. mole^{-1}, log A = 9·75. For *o*-chloro-compounds we evaluate the quantity $\Delta E'$ (obs.) = −2·303 RT [log (k/k_0) − 0·84], where 0·84 is the difference between the log A values for ethyl benzoate (9·75) and ethyl *o*-chlorobenzoate (8·91). By this procedure we exclude from consideration the part of the effect of *o*-Cl which changes the non-exponential factor and we deal only with the part which changes the activation energy. Mean values (over the various experimental temperatures) for $\Delta E'$ (obs.) are shown in Table 6. Values of $\Delta E'$ (pred.) for the dichlorobenzoates are

TABLE 6.

Cumulative effect of chlorine substituents on the alkaline hydrolysis of ethyl benzoate.

Subst.	$\Delta E'$ (obs.)	$\Delta E'$ (pred.)	$\Delta E'$ (obs.) − $\Delta E'$ (pred.)	Departure (%)
2,3-Cl_2	−2320	−2760	+440	−16
2,4-Cl_2	−2510	−2440	−70	+3
2,5-Cl_2	−2840	−2760	−80	+3
3,4-Cl_2	−1860	−2040	+180	−9
3,5-Cl_2	−2380	−2360	−20	+1

$\Delta E'$ (obs.): *o*-Cl, −1580; *m*-Cl, −1180; *p*-Cl, −860.

calculated from $\Delta E'$ (obs.) values for the monochlorobenzoates by assuming a strictly additive effect.

The reaction of substituted benzoyl chlorides with aniline. The Arrhenius non-exponential factor seems unaffected by chlorine atoms in the *ortho*-, *meta*-, or *para*-position of the benzoyl chloride molecule (see p. 4749). The cumulative effect can thus be assessed in a

[25] Kadesch, *J. Amer. Chem. Soc.*, 1944, **66**, 1207.
[26] Newman, "Steric Effects in Organic Chemistry," Wiley, New York, 1956, p. 216.
[27] Tommila, *Ann. Acad. Sci. Fennicae*, 1941, **57**, *A*, No. 13.

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way analogous to that used for the alkaline hydrolysis of *m*- and *p*-chloro-substituted benzoates. Mean values of $\Delta E'$ (obs.) and $\Delta E'$ (pred.) over the four experimental tem-

TABLE 7.

Cumulative effect of chlorine substituents in benzoyl chloride on the reaction with aniline.

Subst.	$\Delta E'$ (obs.)	$\Delta E'$ (pred.)	$\Delta E'$ (obs.) − $\Delta E'$ (pred.)	Departure (%)
2,3-Cl_2	−1050	−1420	+370	−26
2,4-Cl_2	−1010	−1060	+50	−4·5
2,5-Cl_2	−1280	−1420	+140	−10
3,4-Cl_2	−690	−800	+110	−14
3,5-Cl_2	−1060	−1160	+100	−8·5

$\Delta E'$ (obs.): *o*-Cl, −840; *m*-Cl, −580; *p*-Cl, −220.

TABLE 8.

Cumulative effect of chlorine substituents on the dissociation of benzoic acid.

Subst.	ΔpK_a (obs.)	ΔpK_a (pred.)	ΔpK_a (obs.) − $-\Delta pK_a$ (pred.)	Departure (%)
2,3-Cl_2	−1·63 [b]	−1·65	+0·02	−1·2
2,4-Cl_2	−1·54 [b, f]	−1·50	−0·04	+2·7
2,5-Cl_2	−1·66 [b, f]	−1·65	−0·01	+0·6
2,6-Cl_2	−2·56 [a, f, g]	−2·54	−0·02	+0·8
3,4-Cl_2	−0·57 [d]	−0·61	+0·04	−6·5
3,5-Cl_2	−0·78 [c]	−0·76	−0·02	+2·6

ΔpK_a (obs.): *o*-Cl, −1·27; *m*-Cl, −0·38; *p*-Cl, −0·23.[e]

At 0·01M. [b] At 0·001M. [c] At 0·0005M. [d] Ref. 13 (the acid was too insoluble for potentiometric study). [e] Ref. 12. [f] Ref. 5: 2,4-Cl_2, −1·53; 2,5-Cl_2, −1·74; 2,6-Cl_2, −2·62. [g] Ref. 13: 2,4-Cl_2, −1·45; 2,6-Cl_2, −2·39.

peratures are shown in Table 7 (2,6-dichlorobenzoyl chloride being omitted as the cumulative effect of its substituents has been discussed on p. 4751).

The ionisation of benzoic acids. The cumulative effect will be assessed in terms of ΔpK_a (Table 8). Values of ΔpK_a (obs.) from the present work and from earlier work are shown, together with values for ΔpK_a (pred.), calculated from Dippy's results.[12]

Cumulative Effect of Chlorine Substituents in the Three Systems.—The alkaline hydrolysis of ethyl benzoates. The rate coefficients were reproducible within about 2% and it follows that little significance should be attached to departures from additivity of less than about 50 cal. Ethyl 3,5-dichlorobenzoate (Table 6) must be regarded as showing strict additivity. This confirms Brynmor Jones and Robinson's earlier result [2a] and is in accord with the general behaviour of 3,5-compounds; *e.g.*, Brynmor Jones and Watkinson [2c] found strict additivity in the alkaline hydrolysis of ethyl 3,5-dichlorocinnamate. Substituent interaction is at a minimum with this arrangement. The departures from additivity in ethyl 2,4- and 2,5-dichlorobenzoate are possibly just significant, but in comparison with the total substituent effect they do not seem important, amounting to not more than about 3%. Thus in spite of the effect of *o*-Cl on the non-exponential factor, the substituents contribute additively to $\Delta E'$. The departure in the case of ethyl 3,4-dichlorobenzoate is more significant, +180 cal. (−9%), in agreement with Brynmor Jones and Robinson's [2a] earlier result. Brynmor Jones and Watkinson [2c] found a −7% departure in the alkaline hydrolysis of ethyl 3,4-dichlorocinnamate. It seems likely that these departures are due to electrostatic interaction between the C–Cl dipoles, reducing the effect of each upon the activation energy. The observed dipole moment of *o*-dichlorobenzene is 2·33D, compared with a value of 2·70 computed vectorially from that of chlorobenzene, and this was attributed by Smallwood and Herzfeld [29] to electrostatic interaction. Departures from additivity in $\Delta E'$ and in

[29] Smallwood and Herzfeld, *J. Amer. Chem. Soc.*, 1930, **52**, 1919.

dipole moment are of similar magnitude relative to the total substituent effect in each case. The most serious departure occurs in ethyl 2,3-dichlorobenzoate: +440 cal. or −16%; or compared with ethyl 2,5-dichlorobenzoate, +520 cal. or −19%. This large departure from strict additivity is probably due to electrostatic interaction between the C–Cl dipoles, as in the 3,4-compound, combined with an effect arising from three substituents adjacent on the ring. In the discussion of the ionisation of benzoic acids (below) it will be seen that there is a well-established effect in which a 3-substituent presses against a 2-substituent and increases the steric interaction of the latter with the 1-side-chain. It appears likely that an effect of this kind is responsible for some of the departure from additivity in the alkaline hydrolysis of ethyl 2,3-dichlorobenzoate, possibly through a small and experimentally undetectable decrease in the Arrhenius non-exponential factor. The minute reactivity of ethyl 2,6-dichlorobenzoate corresponds to a gross departure from additivity, readily explicable in terms of the chlorine atoms' twisting the side chain and hindering access of the hydroxyl-ion on both sides of the ester group.

The reaction of substituted benzoyl chlorides with aniline. The percentage departures from strict additivity are considerably greater than in ester hydrolysis (Table 7), and with the exception of 2,4-dichlorobenzoyl chloride all the compounds show departures considerably in excess of 50 cal., a reasonable allowance for experimental error. The departure from additivity in 3,5-dichlorobenzoyl chloride is rather unexpected, but there are some cases recorded of departures from strict additivity of substituent effects in 3,5-compounds; *e.g.*, Dippy, Hughes, and Bray [5] find a −32% departure from additivity in the ionisation of 3,5-dihydroxybenzoic acid, which they cannot explain. The poor additivity shown by the dichlorobenzoyl chlorides may possibly be connected with the enhanced rôle of the $+M$ effect of chlorine in the reaction with aniline as compared with the alkaline ester hydrolysis (p. 4749). The breakdown in additivity for $\Delta E'$ may, of course, lie in non-additivity in the changes in activation energy or in the occurrence of small, experimentally undetectable variations in log A. Insofar as the additivity is best with 2,4-dichlorobenzoyl chloride, the unexpected departures in the other compounds seem to be connected with *m*-Cl. While it is probable that this effect is genuine, a spurious effect of this nature would arise from the use of an erroneous $\Delta E'$ (obs.) value for *m*-chlorobenzoyl chloride in the calculation of the values of $\Delta E'$ (pred.). A value for *m*-chlorobenzoyl chloride of −530 cal., instead of −580, would reduce the departure in the 3,5-compound to 0%, in the 2,5-compound to −6·5%, and in the 3,4-compound to −8% (cf. departure in alkaline hydrolysis of ethyl 3,4-dichlorobenzoate). This would imply that the observed rate coefficients for *m*-chlorobenzoyl chloride are some 10% higher than the true values, presumably owing to traces of fast-reacting impurity. Scrutiny of the detailed kinetic results does not, however, reveal any suspicious feature, such as a trend in the rate coefficient over the course of the reaction.

The −14% departure from additivity in 3,4-dichlorobenzoyl chloride suggests that electrostatic interaction between the C–Cl dipoles is responsible for about the same departure as in ester hydrolysis. The departure in the 2,3-compound is about −16% compared with the 2,5-compound, and this is similar to that observed in the hydrolysis of the corresponding esters. The low reactivity of 2,6-dichlorobenzoyl chloride (p. 4749) corresponds to a gross departure from an additive effect of substituents, that is, however, not so serious as in the case of the alkaline hydrolysis of ethyl 2,6-dichlorobenzoate. This is readily explicable in terms of the different transition states and the different ways in which the *o*-chlorine atoms act in the two reactions.

The ionisation of benzoic acids. The substituent effects show good additivity in all six dichlorobenzoic acids (Table 8). Departures of less than 0·04 pK unit are not significant, so none of the departures recorded is more than barely significant, and in all cases the percentage departure is small.

The agreement between observed and predicted values is excellent for the 3,5-acid. In the case of the 2,5-acid the agreement with our ΔpK_a (obs.) is good, but there is a +5%

departure if ΔpK_a (obs.) based on the result of Dippy *et al.*[5] is taken. For the 2,4-acid all the available values of ΔpK_a (obs.) are in reasonable agreement with ΔpK_a (pred.), although the small departure changes sign as between our value and Dippy's on the one hand and Davis and Hetzer's [13] on the other. Thus, on the whole, there is no indication of any serious departures from strict additivity for the 3,5-, 2,5-, and 2,4-acid, and their behaviour is similar to that of the corresponding esters in alkaline hydrolysis.

The most striking feature of Table 8 is the apparent strict additivity shown by the 3,4-, 2,3-, and 2,6-acid. Davis and Hetzer [13] refer to the additivity of substituent effects shown by 3,4-dichlorobenzoic acid. It is difficult, however, to be certain of the exact situation since the total substituent effect is small, and a percentage departure similar to that observed in the alkaline hydrolysis of ethyl 3,4-dichlorobenzoate would correspond to a barely significant departure in terms of pK_a units. The situation is much clearer in the case of 2,3-dichlorobenzoic acid where the total substituent effect is large, and the additivity is certainly much better than that shown in the alkaline hydrolysis of ethyl 2,3-dichlorobenzoate. Thus the effects associated with electrostatic interaction of the C–Cl dipoles and with the three substituents adjacent on the ring are not immediately apparent in the dissociation of benzoic acid. A tentative explanation for this may be advanced. The high ΔpK_a value of *o*- compared with that of *p*-chlorobenzoic acid is due largely to the steric effect of the *o*-chlorine atom, which stabilizes the ion relative to the undissociated acid by twisting the side-chain out of the plane of the ring in both the ion and the acid, thus inhibiting mesomerism involving the interaction of ring and side-chain.[29] The total effect of the substituents in 2,3-dichlorobenzoic acid is thus only partly polar in nature, and departures from additivity due to electrostatic interaction will tend to be obscured. Further, electrostatic interaction of the substituents may be in competition with another factor tending to increase their effect. Dippy *et al.*[30] have shown that 2,3-dimethylbenzoic acid is much stronger than predicted; ΔpK_a (obs.) is −0·37 compared with a ΔpK_a (pred.) value of −0·24. Peltier has shown [31] that several 3-substituted *o*-toluic acids are stronger than the isomeric 5-substituted *o*-toluic acids. Dippy *et al.* have suggested that in 2,3-dimethylbenzoic acid the 3-methyl group presses against the 2-methyl group and thereby increases the steric inhibition of mesomerism of the carboxyl group which is probably responsible for the strengthening effect of an *o*-methyl group. This suggestion is in agreement with Peltier's observation that the discrepancy between the 3- and the 5-substituted acid increases with the bulk of the substituent. It seems probable that such an effect will operate in 2,3-dichlorobenzoic acid but will be in competition with electrostatic interaction tending to reduce the strength of the acid. In the result the two effects appear almost to cancel out, so that 2,3-dichlorobenzoic acid shows good additivity of substituent effects.

In 2,6-dichlorobenzoic acid there is good additivity of substituent effects, as judged both by our value of ΔpK_a (obs.) and by Dippy's value. The additivity is not so good if Davis and Hetzer's value is considered, and these authors suggested that the first *o*-Cl is more effective than the second in enhancing the strength of benzoic acid. In any case the percentage departure from strict additivity is clearly much smaller than for many 2,6-disubstituted benzoic acids, as may be seen from the results of Dippy and his colleagues,[5] Peltier's results,[32] and the data summarised by Shorter and Stubbs.[3] If the effect of *o*-Cl on the strength of benzoic acid is due to a combination of steric and polar factors (see above), then it appears that such factors are additive for two *o*-chlorine atoms. It is surprising that the effect of two *o*-chlorine atoms in twisting the side-chain out of the plane of the ring should be strictly additive as measured by ΔpK_a. (In Shorter and Stubbs's Table [3] 2,4,6-tribromobenzoic acid, however, also shows an additive effect of substituents.)

[29] Newman, ref. 26, p. 429.
[30] Dippy, Hughes, and Laxton, *J.*, 1954, 1470.
[31] Peltier, *Compt. rend.*, 1955, **241**, 57.
[32] Peltier, *Compt. rend.*, 1955, **241**, 1467.

This situation is in sharp contrast to that prevailing in the alkaline hydrolysis of ethyl 2,6-dichlorobenzoate and in the reaction of 2,6-dichlorobenzoyl chloride with aniline.

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UNIVERSITY OF HULL. [*Received, November 18th,* 1960.]

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938. *Oxidations of Organic Compounds with Quinquevalent Vanadium. Part VIII.*[1] *The Oxidation of Oxalic Acid.*

By J. R. JONES and WILLIAM A. WATERS.

Bobtelsky and Glasner [2] reported that the rate of oxidation of oxalic acid by quinquevalent vanadium is diminished by the addition of mineral acid, reaches a minimum value at about 3·5M-[H^+] and thereafter increases. A kinetic study confirms this observation and shows that oxalic acid must form with vanadium(v) a number of complexes of different stabilities. In the absence of mineral acid a complex, vanadium(v),$(H_2C_2O_4)_2$, readily oxidises further oxalic acid. In acid solutions this complex breaks down; in concentrated mineral acid the oxidation becomes a bimolecular reaction between the ion $V(OH)_3^{2+}$ and $H_2C_2O_4$.

PREVIOUS investigations of this series have shown that oxidations of organic compounds by quinquevalent vanadium occur only in acid solution and involve cations, such as VO_2^+ or $V(OH)_3^{2+}$, which first combine with organic substrates to form co-ordinated complexes; these then decompose homolytically, yielding a derivative of quadrivalent vanadium and an organic radical. In general, these oxidations exhibit acid catalysis, the ion $V(OH)_3^{2+}$ being a much more potent oxidant than VO_2^+, and they are of the first order with respect to the organic substrate.

Bobtelsky and Glasner,[2] however, reported that the rate of oxidation of oxalic acid by quinquevalent vanadium can be diminished by addition of hydrochloric or sulphuric acid, reaching a minimum value at about 3·5M-hydrogen ion concentration. They also found that the oxidation was of the first order with respect to vanadium(v), but approximately of the second order with respect to oxalic acid. Since, both the negative acid catalysis and the reaction order with respect to the oxalic acid, appeared to be unique, we have investigated this oxidation in greater detail. Our results, which accord with the account given by Bobtelsky and Glasner, show that the unusual kinetic features of the reaction are due to the formation of a seriex of complexes between vandium(v) and oxalic acid, the stabilities of which are pH-dependent.

RESULTS

The stoicheiometry of the overall reaction accords with the equation

$$2V^{V} + H_2C_2O_4 = 2V^{IV} + H_2O + 2CO_2$$

but we have been unable to adduce any experimental evidence of the transient formation of organic radicals, or of radical-ions such as $HC_2O_4^{\cdot}$, $\cdot C_2O_4^{-}$ or $\cdot CO_2^{-}$, since the mixture formed during this oxidation of oxalic acid, unlike those given by manganic salts [3] or by Fenton's reagent,[4] does not promote the chain reaction between oxalic acid and mercuric chloride or

[1] Part VII, *J.*, 1961, 630.
[2] Bobtelsky and Glasner, *J. Amer. Chem. Soc.*, 1942, **64**, 1462.
[3] Drummond and Waters, *J.*, 1953, 2836.
[4] Weiss, *Discuss. Faraday Soc.*, 1947, **2**, 188.

the polymerisation of vinyl cyanide. However, we do not consider that this negative evidence of radical formation necessarily indicates that a 2-electron oxidation, such as

$$V^{V} + H_2C_2O_4 \xrightarrow[\text{Slow}]{} V^{III} + 2H^{+} + 2CO_2$$

$$V^{III} + V^{V} \xrightarrow[\text{Fast}]{} 2V^{IV}$$

is involved; the oxalic acid radical may be oxidised so rapidly by V^{V} that its independent existence cannot be demonstrated by the tests mentioned above.

The oxidations of oxalic acid by vanadium(v) were all carried out in solutions in which

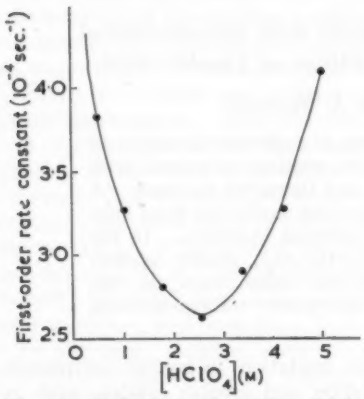


FIG. 1. Oxidation of oxalic acid in perchloric acid at 50°.

$[V^{V}] = 0{\cdot}05$M. $[H_2C_2O_4] = 0{\cdot}122$M. Ionic strength = 5·1.

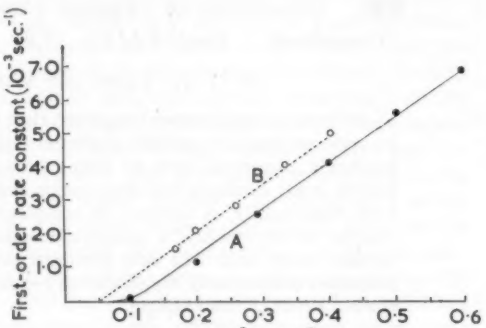


FIG. 2. Oxidation of oxalic acid at 40° in the absence of mineral acid.

Ionic strength = 2·1. (A) Initial $[V^{V}] = 0{\cdot}05$M. (B) Initial $[V^{V}] = 0{\cdot}025$M.

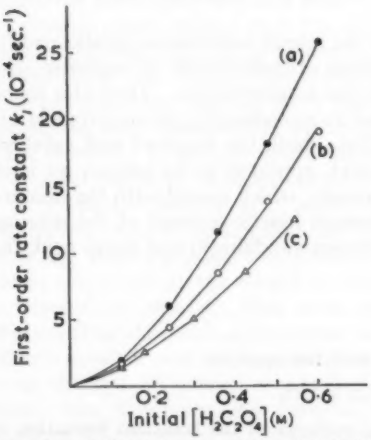


FIG. 3. Oxidation of oxalic acid at 40° in dilute perchloric acid.

Initial $[V^{V}] = 0{\cdot}05$M. (a) $[HClO_4] = 0{\cdot}50$M; ionic strength = 3·1. (b) $[HClO_4] = 1{\cdot}00$M; ionic strength = 3·1; (c) $[HClO_4] = 1{\cdot}45$M; ionic strength = 3·55.

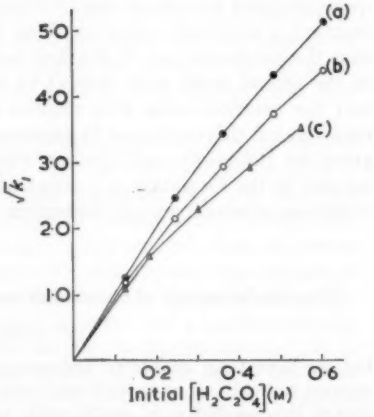


FIG. 4. Curves of Fig. 3 plotted to show the approximation to a second-order rate-dependence on oxalic acid.

oxalic acid was present in large excess over vanadium and were all found to follow strict first-order kinetics with respect to the vanadium for at least 85% of the oxidation.

The general trend of the oxidation in the presence of perchloric acid is shown by Fig. 1. Fig. 2 shows the relation between the rate of oxidation and the initial concentration of the oxalic acid in solutions made up from ammonium metavanadate with no added mineral acid; the curves of Fig. 3 show corresponding rates of oxidation in the presence of 0·5M-, 1·0M-, and 1·45M-perchloric acid respectively. Fig. 4 shows that the results plotted in Fig. 3 correspond approximately to a reaction having second-order kinetics with respect to total oxalic acid concentration, especially at the lower values, and explains how Bobtelsky and Glasner came to their conclusions mentioned above.

Table 1 shows that, in the absence of mineral acid, ammonium oxalate can replace oxalic acid and also that the addition of 0·10M-perchloric acid has very little effect on the oxidation rate. Table 2, however, shows how slightly larger amounts of perchloric acid decrease the oxidation rate when an excess of oxalic acid is present.

It is clear, from Fig. 2, that in the pH range 1—2 a complex of vanadium(V) with two molecules of oxalic acid must be reacting with a third molecule of oxalic acid before any vanadium(IV) is formed, but the potentiometric titration of oxalic acid with alkali in the presence of ammonium metavanadate (Fig. 5) shows that the complex formation effects no significant pH change in this region.

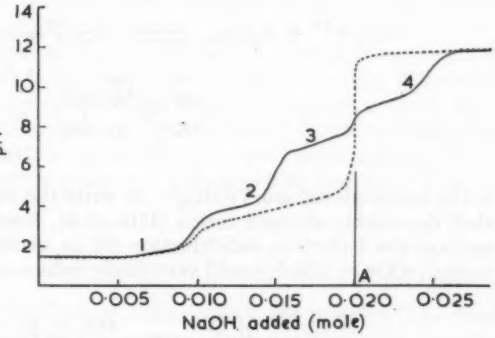


FIG. 5. Potentiometric titration of oxalic acid and its vanadium(V) complexes.

Full line: The initial solution contained 0·01 mole of oxalic acid (0·20M) and 0·0025 mole of ammonium metavanadate (0·05M). Broken line: The initial solution contained 0·01 mole of oxalic acid (0·20M) only. The titration was carried out with 1·0M-sodium hydroxide.

Fig. 3 indicates that the vanadium(V)–oxalic acid complex, formed in neutral solution, breaks down gradually to other complexes as the acidity of the medium is increased; and finally Table 3 indicates that at high acidity (4·2M) the reaction approaches one of first order

TABLE 1.

Oxidation of oxalic acid by aqueous ammonium metavanadate (0·05M) at 40°.
Ionic strength of all solutions, 2·1.

	First-order rate constants, k_1 (10^{-3} sec.$^{-1}$)		
Oxalic acid (M)	Only $NaClO_4$ added	$(NH_4)_2C_2O_4$ added (0·05M)	$HClO_4$ added (0·10M)
0·101	0·125	0·320	0·22
0·201	1·18	1·77	1·08
0·401	4·15	—	4·17

TABLE 2.

Effect of varying perchloric acid concentrations in the range 0·0—1·0M.

$[V^V]$ = 0·05M. $[H_2C_2O_4]$ = 0·121M. Ionic strength = 2·1. Temp. = 40°.

$[HClO_4]$ (M)	0·00	0·10	0·20	0·30	0·40	0·50	0·80	1·0
10^4k_1 (sec.$^{-1}$)	3·17	2·92	2·50	2·22	1·98	1·83	1·60	1·44

TABLE 3.

Reaction order with respect to oxalic acid in 4·2M-perchloric acid at 50°.

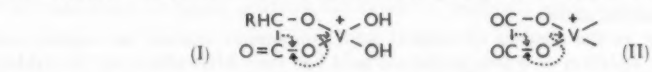
$[V^V]$ = 0·05M. Ionic strength = 5·1.

Oxalic acid (M)	0·024	0·049	0·073	0·097	0·122
$10^3k_2 = k_1/[H_2C_2O_4]$	2·17	2·29	2·42	2·60	2·71

with respect to oxalic acid even at low concentrations of the latter. As Fig. 1 shows, the oxidation then becomes an acid-catalysed process, just as would be expected for a reaction involving $V(OH)_3^{2+}$ rather than VO_2^+.

Discussion

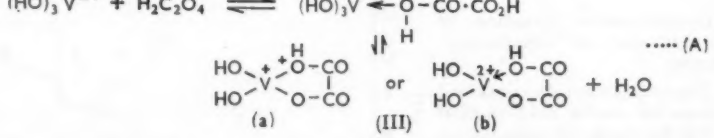
Other studies [1,3] of oxidations of organic molecules by vanadium(v) have indicated that formation of a cyclic transition complex (*e.g.*, I) favours the movement of an electron to a positively charged vanadium centre. Consequently, for oxidation of oxalic acid one



(I) (II)

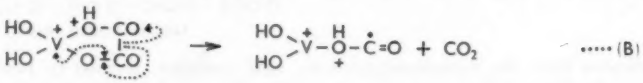
may suggest that the oxidisable complex is more likely to contain the cyclic group (II) than a linear group HO·CO·CO·V< in which there is no structural assistance to 1-electron movement.

Now at acidities over 4N with respect to hydrogen ion the oxidation of oxalic acid appears to be a reaction of normal type, *i.e.*, of the first order with respect to both $[H^+]$ and [Oxalic acid]. Under these conditions it is rational to consider that the active oxidant



..... (A)

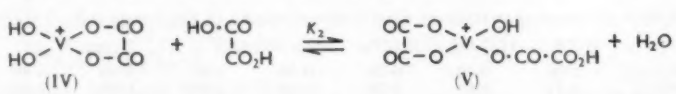
is the uncomplexed ion $V(OH)_3^{2+}$, to write the equilibria as annexed (A), and to suggest that the doubly charged cation (IIIa or b), formed to a slight extent only, can readily undergo the 1-electron redistribution (B) to a compound of vanadium(IV) having a bound radical, ·CO·O–, which would very easily reduce another ion of vanadium(v).



..... (B)

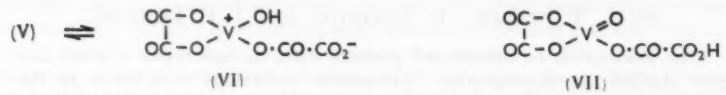
As the acidity is lowered the cation (III), being a strong acid, would lose proton giving a complex (IV) which can also be formed by combination of oxalic acid and the abundantly present ion VO_2^+. Since VO_2^+ is but a feeble oxidant, the ion (IV) can be regarded as a stable complex, whilst again the equilibrium constant K_1, which must be acid-dependent, may be small at hydrogen-ion concentrations over 1·0N.

However, at lower acidities the hydroxyl groups of the ion (IV) may react with a further molecule of oxalic acid, and, since the carboxyl group is electrophilic, complex (V) would be less stable than complex (IV) and may decompose as shown.



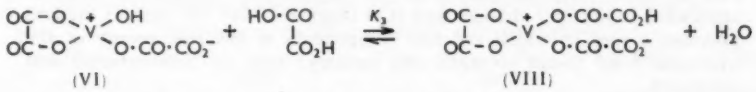
Under conditions in which both K_1 and K_2 are small, we have [(IV)] = approx. $K_1[VO_2^+][H_2C_2O_4]$ and [(V)] = approx. $K_1K_2[VO_2^+][H_2C_2O_4]^2$, so that the decomposition of the complex ion (V) could appear to be roughly of the second order with respect to oxalic acid. More exactly, however, the kinetics appertaining to the slow decomposition of the complex (V) would accord with the experimental data shown in Fig. 3.

As the acidity is lowered still further, oxalic acid would begin to ionise, and so likewise would the acid complex (V); the latter would then give an electrically neutral complex



(VI) (VII)

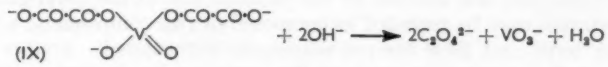
(VI or VII) in which the electron-attracting properties of the vanadium atom would be very small. The tendency of this complex to lose oxalic acid would also diminish as the environment becomes more neutral. However, it may combine with yet another molecule of oxalic acid:



(VI) (VIII)

and since Fig. 2 shows that a complex of formula $(H_2C_2O_4)_2,V^V$ is an oxidant of oxalic acid it may be concluded that a cyclic ternary complex such as (VIII) easily decomposes to a compound of vanadium(IV). This is rational since complex (VIII), unlike (VII), necessarily has a positively charged vanadium at its centre.

Our present evidence indicates that oxidation of oxalic acid is possible down to pH 2, but does not occur at still lower acidities. The potentiometric titrations (Fig. 5) indicate that the dissociation constant of a complex (VI) is of the same order as that of oxalic acid, but that in the pH range 2—6 another complex, *e.g.*, (IX) is formed which consumes two equivalents of alkali in decomposing to free oxalate, $C_2O_4^{2-}$, and metavanadate, VO_3^-, anions which are present at the equivalence point A. This neutralisation (part 3 of the curve) can be represented as:



(IX)

Since in this pH range there is no reduction of vanadium(V), the complex (IX) must be stable to reduction by oxalate anions. The four sections of the potentiometric titration curve thus represent:

$$(1)\quad H_2C_2O_4 + OH^- \rightleftharpoons HC_2O_4^- + H_2O$$
$$(VII, VI) + 3OH^- \rightleftharpoons (IX) + 2H_2O$$
$$(2)\quad 2HC_2O_4^- + 2OH^- \rightleftharpoons 2C_2O_4^- + 2H_2O$$
$$(3)\quad (IX) + 2OH^- \rightleftharpoons 2C_2O_4^- + VO_3^- + H_2O$$
$$(4)\quad VO_3^- + OH^- \rightleftharpoons HVO_4^{2-}$$
$$NH_4^+ + OH^- \rightleftharpoons NH_3 + H_2O$$

Experimental

Standardised solutions of " AnalaR " oxalic acid were used. Vanadium(V) solutions were made up, as in previous work, from " AnalaR " ammonium metavanadate and " AnalaR " perchloric acid; " recrystallised grade " sodium perchlorate (Hopkin and Williams) was used for adjustment of ionic strengths.

Reactions, carried out in a thermostat regulated within $\pm 0{\cdot}1°$, were followed titrimetrically as in Part I,[5] but care was taken not to expose solutions containing ferric oxalate (formed by the quenching of V^V with Fe^{2+}) to direct sunlight in which this salt quickly decomposes regenerating Fe^{2+}. If such solutions had to be retained for more than a few minutes they were stored in the dark. The rates of the direct oxidations of oxalic acid by vanadium(V) were not affected by exclusion of light.

Potentiometric titrations were made at room temperature with a Doran pH meter with one glass electrode and one saturated calomel electrode in the titration vessel.

The Dyson Perrins Laboratory, Oxford. [*Received, April 27th*, 1961.]

[5] Littler and Waters, *J.*, 1959, 1299.

939. *The Association of* ortho-*Substituted Phenols with Ethers.*

By L. J. Bellamy, G. Eglinton, and J. F. Morman.

The association of substituted phenols with various types of ether has been studied spectroscopically. Systematic variations were made in the numbers and sizes of the alkyl substituents of the phenols and of the ethers. The results show that with minor exceptions (particularly 2,6-di-t-butylphenol) changes in the sizes of the substituents do not materially affect the strength of the hydrogen bond formed, as measured by $\Delta\nu$(OH), but do lead to quite large alterations in the equilibrium coefficients. This is attributed to entropy changes and it is suggested that the present method provides a way in which the two components of the free energy of the hydrogen bond (bond strength and entropy) may be differentiated and compared.

There have been several spectroscopic studies on " hindered phenols," which are generally regarded as all those with 2,6-dialkyl substituents. Most of these have been concerned with the liquid or the solid phase in which the stretching frequencies of the associated hydroxyl groups occur at higher values than in normal phenols.[1-3] This is ascribed to steric effects which limit the association to weakly bonded dimers instead of the usual polymers. Puttnam [2] suggested that steric effects may also occur in *o*-t-butylphenol as this compound shows two free ν(OH) bands in solution which could be derived from *cis*- and *trans*-arrangements of the H–O–Ph group with respect to the *o*-alkyl substituent.

In contrast, Bellamy and Williams [3] have shown that the relative strength of the hydrogen bonds formed between solvents and mono- or di-*o*-alkylphenols (other than 2-6-di-t-butylphenol) are not affected by the physical size of the alkyl group. The free energy of association may be regarded as composed of two components, a bond strength and an entropy term, and these are not necessarily interrelated. Studies of the equilibrium coefficient K provide a measure of the whole, whilst frequency shifts provide a measure only of the first term as they are determined by the changes in the O–H bond stretching force constant.

From studies on both K and $\Delta\nu$ it should, therefore, be possible to differentiate between two different kinds of steric effect. There are those—here termed " physical " effects—which lead to a reduction in the force constant of the hydrogen bond due to an otherwise unnatural O · · · O distance, and those which arise simply from variation in the entropy term. It is, for example, possible to envisage a series of different compounds, all forming hydrogen bonds of the same strength with a given acceptor, but showing variations in their equilibrium coefficients because steric effects influence the ability of the hydrogen bond, once broken, to be re-formed with consequent change in the entropy term.

We have therefore studied the association of a range of *ortho*-substituted phenols with ethers which themselves comprise alkyl groups of various sizes. Bistrimethylsilyl oxide with an Si–O–Si angle [4] of 130° has been included as being somewhat similar in shape to di-t-butyl ether and as being likely to produce considerable steric effects. It was hoped in this way to decide the sizes of the groups necessary for a measurable change in the O · · · O distance. At the same time we measured the equilibrium coefficients for the association of the phenols with ethers, in a standard solvent under fixed conditions, in order to measure the total free-energy change.

[1] Sears and Kitchen, *J. Amer. Chem. Soc.*, 1949, **71**, 4110; Coggeshall, *ibid.*, 1947, **69**, 1620; 1950, **72**, 2836; Coggeshall and Saier, *ibid.*, 1951, **73**, 5414; Friedel, *ibid.*, 1951, **73**, 2881.
[2] Puttnam, *J.*, 1960, 486, 5100.
[3] Bellamy and Williams, *Proc. Roy. Soc.*, 1960, *A*, **254**, 119.
[4] Yamasaki, Kotera, Yokoi, and Ueda, *J. Chem. Phys.*, 1950, **18**, 1414; Roth, *Ann. Rev. Phys. Chem.*, 1951, **2**, 217.

Experimental

The materials were of commercial origin, except di-t-butyl ether,[5] 2,6-diethylphenol,[3] *o*-t-butylphenol, and bistrimethylsilyl oxide, the last two kindly supplied respectively by Mr. Ivor Brown and Dr. Vincent Davies of Imperial Chemical Industries Limited. The compounds were purified, dried, and checked by gas–liquid chromatography before use.

Spectra were recorded linearly in cm.$^{-1}$ as percentage transmission with a Unicam S.P. 100 double-beam infrared spectrophotometer equipped with an S.P. 130 sodium chloride prism-grating double monochromator [3000 lines per in. (2000—3656 cm.$^{-1}$)] operated under both

Table 1.

Hydroxyl stretching frequencies (cm.$^{-2}$) of alkyl-substituted phenols.

(Apparent extinction coefficients, ε_a, in parentheses.)

State/Subst.	None	2-Me	2-Pr^i	2-Bu^t	2-Bu^t, 5-Me
Vapour †	3654	*	3654	*	*
Liquid	—	—	—	~3600sh	3606
	~3510sh	~3550sh	3533sh	3535	3528
	~3350br	~3395br	3460br	Tail	Tail
Hexane	3622	3623	3625	3655 3616	3655 3616
CCl_4	3612(205)	3613(165)	3615	3647(25) 3606(200)	3647(15) 3608(170)
Tetrahydrofuran	3287vbr †	3304(175)	3303 †	3299(180)	3307(180)
Diethyl ether	3344 †	3341(165)	3338 †	3337(170)	3343(170)
Di-isopropyl ether	3625vw	3627vw	3620vw	—	
	3329(180)	3332(160)	3330(160)	3324(175)	3335(160)
Di-n-butyl ether	3620vw	3620vw	3622(5)	3613vw	3615(5)
	3336(170)	3345(140)	3341(145)	3338(165)	3342(155)
				3650vw	
Di-t-butyl	3618vw	3623(10)	3613vw	3613vw	3613vw
	3306(130)	3318(115)	3310(120)	3305(120)	3314(55)
				3655(15)	*
Bistrimethylsilyl oxide	3621(80)	3623(80)	3621(75)	3615(70)	3616(75)
	3448(80)	3456(45)	3449(55)	3442(65)	3451(55)

State/Subst.	2,6-Me$_2$	2,6-Et$_2$	2,6-Pr$^i_2$	2,6-Bu$^t_2$	4-Me, 2,6-Bu$^t_2$
Vapour †	3654	3652	3650	*	3671
Liquid	—	3622sh †	3618	3644	3648 †
	3573	3583 †	3577	—	—
	3500sh	*	Tail	—	—
Hexane	3629	3629	3627 3642sh	3653	3655
CCl_4	3621(155)	3623	3620(145)	3647(240)	3651
Tetrahydrofuran	3503vwsh †			3641(45)	3645,† 3536 †
	3383br †	3405br †	3410 †	3545(70)	3400 †
Diethyl ether		3620 †	3624 †	3649(115)	3651 †
	3407 †	3412 †	3428 †	3385(25)	
Di-isopropyl ether	3629(15)	3629(20)	3629(20)	3650(155)	3654(145)
	3398(90)	3400(90)	3410(85)	3404vw	3450(10)
Di-n-butyl ether	3628(15)	3627(25)	3625(30)	3650(150)	3651(145)
	3407(85)	3421(75)	3435(65)	3383vw	3405(10)
Di-t-butyl ether	3629(40)	3628(45)	3627	3651(200)	3654(195)
	3418(60)	3424(60)	3425	—	3475(5)
Bistrimethylsilyl oxide	3627(110)	3628(130)	3627(125)	3653(160)	3654(215)
	3545(15)	—	—	—	—

* Not measured. — No absorption. Tail = absorption diminishing slowly towards lower frequencies. † Values taken from ref. 3.

dry-air and vacuum conditions. The wave-number scale calibration was checked against the spectra of water vapour and ammonia before and after each interrupted group of measurements. Frequency measurements for the " free " and ether-associated hydroxyl bands are believed to be accurate to ± 1 and ± 2 cm.$^{-1}$, respectively.

The linearity of the percentage transmission scale was checked by Shrewsbury's procedure,[6] and

[5] Erickson and Ashton, *J. Amer. Chem. Soc.*, 1941, **63**, 1769.
[6] Shrewsbury, " Unicam Spectrovision," 1958, No. 6, p. 1.

intensities were measured on bands of $\leqslant 10\%$ transmission. The theoretical spectral slit-width, computed from tables supplied by Unicam Instruments Ltd., was approximately 5·5 cm.$^{-1}$ at 3600 cm.$^{-1}$, and 4·5 cm.$^{-1}$ at 3350 cm.$^{-1}$. The region 300—3660 cm.$^{-1}$ was scanned at 33 cm.$^{-1}$ per min. and the " free " hydroxyl bands near 3600 cm.$^{-1}$ were scanned for a second time at 16 cm.$^{-1}$ per min. Intensities are given as apparent extinction coefficients ε_a (l. mole^{-1} cm.$^{-1}$) rounded to the nearest 5 units and measured from a solvent–solvent base-line superimposed on the record of the absorption of the solution (determined with solvent in the reference beam). The integrated absorption intensities, A and $A°$ (Table 2), of the free hydroxyl bands were calculated

TABLE 2.

Integrated absorption intensity data (A) for hydroxyl stretching bands of *o*-alkylphenols in 0·5M-ether–carbon tetrachloride solution.

Subst.:		None		2-Me		2-Pr^i		2-Bu^t	
Dissolved ether		ν(OH)	$10^{-4}A$	ν(OH)	$10^{-4}A$	ν(OH)	$10^{-4}A$	ν(OH)	$10^{-4}A$
Tetrahydrofuran	free	3611	0·225	3613	0·310	3612	0·280	3647	0·075
								3606	0·275
	assoc.	3321	9·00	3329	8·85	3329	8·70	3332	8·60
Diethyl ether	free	3611	0·345	3613	0·410	3613	0·400	3648	0·095
								3607	0·360
	assoc.	3334	7·30	3340	6·65	3340	6·25	3338	6·20
Di-isopropyl ether	free	3611	0·300	3613	0·430	3612	0·400	3647	0·080
								3607	0·335
	assoc.	3314	8·00	3322	7·00	3325	7·00	3325	7·10
Di-n-butyl ether	free	3612	0·390	3614	0·510	3613	0·430	3648	0·100
								3607	0·410
	assoc.	3330	6·65	3335	5·80	3336	5·35	3336	5·95
Di-t-butyl ether	free	3610	0·450	3613	0·590	3612	0·575	3648	0·105
								3607	0·505
	assoc.	3297	7·35	3314	5·90	3325	5·85	3336	5·05
Bistrimethylsilyl oxide	free	3611	1·00	3613	1·10	3612	1·10	3648	0·170
								3607	0·945
	assoc.	3454	1·85	3464	1·45	3462	0·650	3447	0·780

Subst.:		2,6-Me$_2$		2,6-Pr$^i_2$		2,6-Bu$^t_2$	
Dissolved ether		ν(OH)	$10^{-4}A$	ν(OH)	$10^{-4}A$	ν(OH)	$10^{-4}A$
Tetrahydrofuran	free	3619	0·490	3618	0·520	3647	1·45
	assoc.	3400	4·30	3426	3·45	3557	0·530
Diethyl ether	free	3620	0·710	3619	0·740	3647	1·35
	assoc.	3409	2·35	3436	2·05	—	
Di-isopropyl ether	free	3620	0·725	3619	0·765	3647	1·25
	assoc.	3395	2·15	3412	1·65	—	
Di-n-butyl ether	free	3620	0·720	3619	0·830	3647	1·30
	assoc.	3401	1·80	3426	1·75	—	
Di-t-butyl ether	free	3621	0·845	3619	0·845	3648	1·30
	assoc.	3424	1·35	3430	0·985	—	
Bistrimethylsilyl oxide	free	3621	0·925	3619	0·895	3648	1·20
	assoc.	—		—		—	

Apparent half-band widths were as follows: free OH bands, 18 $\pm$ 2 cm.$^{-1}$, except the band near 3650 cm.$^{-1}$ in *o*-t-butylphenol (~24 $\pm$ 1 cm.$^{-1}$); associated OH bands varied from 150 to 270 cm.$^{-1}$ with no apparent regularity.

The integrated absorption intensities of the phenols in CCl_4, $10^{-4}A°$, were phenol 1·20, 2-Me 1·05, 2-Pr^i 1·10, 2-Bu^t 0·95, 2,6-Me$_2$ 0·95, 2,6-Pr$^i_2$ 0·90, and 2,6-Bu$^t_2$-phenol 1·30.

by the method of direct integration due to Ramsay [7] and are in l. mole^{-1} cm.$^{-2}$. Approximate integrated absorption intensities, A, of the more asymmetrical, associated hydroxyl peaks were obtained by averaging areas calculated by use of $\Delta\nu_{\frac{1}{2}}{}^a$, $\Delta\nu_{\frac{1}{3}}{}^a$, and $\Delta\nu_{\frac{1}{4}}{}^a$, according to the improved, direct, integrated-intensity measurement technique of Cabana and Sandorfy.[8]

For the determination of K values (Table 3) for the association of the phenols with the ethers in the mixed solvents, the solutions in carbon tetrachloride were 0·1 $\pm$ 0·002M with respect to the phenols and 0·5 $\pm$ 0·002M with respect to the ethers. In such solutions there is very little self-association and it is reasonable and convenient to assume that only phenol–ether interactions are involved. Measurements were made immediately after the solutions

[7] Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72.
[8] Cabana and Sandorfy, *Spectrochim. Acta*, 1960, **16**, 335.

had been prepared, the same pair of cells being used throughout. The solutions were allowed to reach the temperature (29° ± 2°) of the sample well of the instrument before the spectra were recorded. Solvent–solvent backgrounds were run immediately before every determination.

$A°$ values were determined for CCl_4 solutions in 5 mm. cells, and at 0·003M-concentration to ensure that all the phenol present was in the monomer form. The proportion of free phenol in the mixed solvents was determined by parallel measurements on the unassociated hydroxyl band. This involves the assumption that the presence of the small amount of ether will not change the absolute integrated intensity, A, of the unassociated band. This is reasonable in view of the small concentration of the ethers and of the fact that the unassociated hydroxyl frequencies are the same as they are in pure CCl_4 solution (Tables 1 and 2). Graphical separation of the bands was unnecessary (cf. Figure).

The K values (l. mole^{-1}) were determined from $A°$ and A as follows:

For acid (a) and base (b) association,

$$a + b \rightleftharpoons a \cdots b,$$

the equilibrium constant $k = [a \cdots b]/[a][b]$.

Then, if c_a = total concentration of acid (mole l.$^{-1}$), c_b = total concentration of base (mole l.$^{-1}$), $A°$ = integrated intensity of ν(OH) in CCl_4 (all " free," *i.e.*, equivalent to A values at zero ether concentration), and A = integrated intensity of ν(OH) free (unassociated) in the mixed ether–CCl_4 solvent, then

$$k = \frac{1 - A/A°}{A/A°[c_b - c_a(1 - A/A°)]}$$

Results.—The results are summarised in Tables 1—3 and illustrated in the Figure. Table 1 gives the values of ν(OH) of the various phenols in various states and in the ethers; Table 2 covers dilute solutions of phenols in binary mixtures of ethers and carbon tetrachloride. Table 3 lists the Δν values and the equilibrium coefficients for many of these systems, under conditions of arbitarily fixed concentrations and temperature.

TABLE 3.

Equilibrium constants (K) * for phenol–ether association at 29° ± 2°.

Hydroxyl frequency shifts, $\Delta\nu = \nu_{OH}^{hexane} - \nu_{OH}^{ether/CCl_4}$, are in parentheses.

	Ether					
Subst.	THF †	Et_2O	Pr^i_2O	Bu^n_2O	Bu^t_2O	$(Me_3Si)_2O$
None	10·4(301)	6·0(288)	7·2(308)	4·9(292)	3·9(325)	0·4(168)
2-Me	5·5(294)	3·4(283)	3·2(301)	2·6(288)	1·7(309)	0(159)
2-Pr^i	6·7(296)	3·9(285)	3·9(300)	3·0(289)	2·0(300)	0·06(163)
2-Bu^t ‡	5·7(284)	3·7(278)	4·1(291)	2·9(280)	2·3(280)	0(169)
2,6-Me_2	2·0(229)	0·67(220)	0·62(234)	0·63(228)	0·22(205)	0·03(—)
2,6-Pr^i_2	1·7(201)	0·51(191)	0·48(215)	0·23(201)	0·19(197)	0·06(—)

* l. mole^{-1}. † Tetrahydrofuran. ‡ Calculations involve band at 3610 only.

K values for 2,6-Bu^t_2 phenol are all approx. zero.

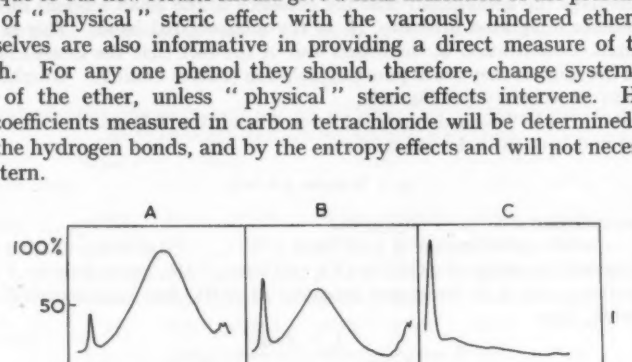
The extremely weak associated hydroxyl absorptions for 2,6-dimethylphenol and 2,6-di-iso-propylphenol in 0·5M-$(Me_3Si)_2O$–CCl_4 could not be accurately located and are not quoted. For the same reason, Δν values are not available for 2,6-di-t-butylphenol in any of the 0·5M-ether–CCl_4 solvents.

DISCUSSION

The proton-donor and -acceptor properties in an acid–base system will determine a characteristic O–H · · · O distance for the hydrogen bond. This may then be modified by any steric effects operating from either side. The Δν values of ν(OH) are directly related to the final O · · · O distances,[9] and therefore provide a guide to the resultant of these effects. With unhindered phenols, it is known that the hydroxyl frequencies vary systematically with the basicity of the solvent in such a way that the Δν/ν values of any one donor in a series of solvents can be plotted directly against the corresponding values of any other in the same solvents, to give a straight line.[3] In any instance in which steric

[9] Nakamoto, Margoshes, and Rundle, *J. Amer. Chem. Soc.*, 1955, **77**, 6480.

effects lead to a larger O···O distance than would be expected from the acid–base properties, a deviation from this straight line will occur, and in principle it should be possible to derive the change in O···O distance which has resulted. It has already been shown in this way that 2,6-di-t-butylphenol is subject to considerable steric hindrance to solvent association, but that other 2,6-dialkylphenols give normal plots.[3] Application of this technique to our new results should give a clear indication of the presence or absence of this kind of "physical" steric effect with the variously hindered ethers. The $\Delta\nu/\nu$ values themselves are also informative in providing a direct measure of the hydrogen bond strength. For any one phenol they should, therefore, change systematically with the basicity of the ether, unless "physical" steric effects intervene. However, the equilibrium coefficients measured in carbon tetrachloride will be determined both by the strengths of the hydrogen bonds, and by the entropy effects and will not necessarily follow the same pattern.



Hydroxyl absorptions of (A) phenol, (B) 2,6-dimethylphenol, and (C) 2,6-di-t-butylphenol (0·1M; in 0·5 mm. cells) in (1) 0·5M-tetrahydrofuran–CCl_4, (2) 0·5M-di-isopropyl ether–CCl_4, and (3) 0·5M-di-t-butyl ether–CCl_4.

$\Delta\nu/\nu$ *Plots.*—The data for the solvent shifts of ν(OH) for many of the phenols now studied are already available.[3] Inclusion of the new data in Tables 1 and 2 on the original plots (Fig. 1 of ref. 3) shows that in the great majority of cases the points fall on the lines within the limits of experimental error. 2,6-Di-t-butyl phenol, of course, shows marked steric effects with all the ethers studied, and none of the 2,6-dialkylphenols associates to an appreciable extent with bistrimethylsilyl oxide, although the monoalkylphenols associate normally. However, only in the case of di-t-butyl ether does there appear to be any other steric hindrance effect resulting in weaker hydrogen bonds, and even this is small The point for *o*-isopropylphenol in this solvent is very slightly displaced from the standard line, in a direction indicating an increased O···O distance, and the effect increases with the degree of substitution of the phenol. However, the effect is not large and even in the more hindered phenols the displacement is only slightly greater than the experimental error. Clearly, the steric effects on the hydrogen-bond strength are too uncommon in

this series, and too small, to be capable of interpretation in terms of the alterations they produce in the O · · · O distances.

Δν *Values.*—For unhindered phenols the Δν values vary systematically with the basicity of the ethers and follow the same order as phenol itself, *i.e.*, $Bu^t_2O > Pr^i_2O >$ Tetrahydrofuran $> Bu^n_2O > Et_2O \gg (Me_3Si)_2O$. Table 3 shows that this order is effectively maintained for all the phenols up to the 2,6-di-t-butyl derivative, the only exception being with di-t-butyl ether. This ether moves down the list as an effective acceptor as the sizes of the substituents of the phenol are increased, a result in line with the findings given above. Exceptionally, in the silyl ether the changes in Δν values are all small, indicating that the hydrogen bonds formed are of comparable strengths.

The slopes of the Δν/ν curves for 2,6-dialkylphenols show them to be less acidic than either phenol or its monoalkyl derivatives. This is reflected in the Δν values in ether, which are smaller by some 60—70 cm.$^{-1}$. This change is too great to be attributed wholly to the inductive effects of the alkyl groups, and in the absence of " physical " steric hindrance it must arise from some dipolar interaction between the hydroxyl and the alkyl groups which reduces the acidity of the former.

The Δν values for the liquid phenols are also of interest (Table 1). Mono-*o*-alkylphenols (with the exception of a t-butylphenol) show values typical of the usual polymeric self-association, but as earlier workers have found, 2,6-dialkylphenols show only small shifts (~45 cm.$^{-1}$) away from the monomeric value. If it is accepted that 2,6-diisopropylphenol is able to form strong hydrogen bonds with say di-isopropyl ether, it is difficult to see why the dialkylphenols should not self-associate freely. Indeed, it would seem that they do (with the exception of 2,6-di-t-butylphenol), at least as far as the dimer stage, as the Δν values are normal for dimeric association when account is taken of their reduced acidity. According to Puttnam [2] the Δν value for liquid dimeric phenol is 107 cm.$^{-1}$ and that of the 2,6-dialkyl dimers is about 65 cm.$^{-1}$. The ratio is almost exactly that which would be predicted from the Δν/ν plots [3] based on associations with solvents with which no " physical " steric hindrance occurs, and in which the differences in Δν values arise solely from acidity effects. Further the Δν values and therefore the hydrogen bond strengths, of 2,6-dimethyl-, 2,6-diethyl-, and 2,6-di-isopropyl-phenol are all essentially the same and do not show the regular changes which might be expected from a change in the steric hindrance. The problem appears to be, therefore, not one of whether these materials are able to self-associate, but why, having done so, they are unable to continue the process by the addition of further units. This problem is intimately connected with the reasons for the strengthening of the hydrogen bonds in polymeric as against dimeric alcohols. Weltner and Pitzer [10] and Pauling [11] suggested many years ago that polymeric alcohols and phenols took a cyclic structure and that the bonds were stronger than those of the dimer for this reason. The present findings also appear to support this view. In the association of say, 2,6-di-isopropylphenol, any " physical " steric hindrance present would be limited to the interaction between one of the isopropyl groups of each unit. No greater interaction could arise to prevent the addition of a third unit to form a trimer, unless this unit were seeking to make up a cyclic system. In the last case, steric interactions would be operating on the isopropyl groups on both sides of the third unit and could well prevent further association. We therefore conclude that dimeric association occurs normally in these phenols and that the differences between them and normal phenols arise from their inability to take up cyclic polymeric forms.

Equilibrium Coefficients.—In the present studies the concentrations of the phenol and ether components in carbon tetrachloride have been maintained at arbitary values, as has the temperature. The observed equilibrium coefficients will depend upon (*a*) the strength of the hydrogen bonds which determine how readily the bonds will be broken and (*b*) the entropy effects which are related to the readiness with which a broken bond will be

[10] Weltner and Pitzer, *J. Amer. Chem. Soc.*, 1951, **73**, 2606.
[11] Pauling, " Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, 3rd edn., 1960, p. 474.

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re-formed. Under the conditions chosen the number of collisions between phenol and ether molecules at any one moment will be more or less the same in all cases. The variations in entropy arise from the fact that the shapes of the donor and the acceptor molecule play a large part in determining what proportion of the collisions leads to hydrogen-bond formation. Large differences due to this effect have already been demonstrated qualitatively in this series.[3]

The experimental values of K for the chosen conditions are given in Table 3; they follow a consistent pattern. For any one phenol the K values do not follow in any way the basicity of the ethers, as do the $\Delta\nu$ values, but instead arrange themselves in the order of the steric complexity of the ethers. The order of effectiveness in maintaining the hydrogen bond is, therefore, tetrahydrofuran $>$ Et_2O,Pr^i_2O $>$ Bu^n_2O $>$ Bu^t_2O $\gg$ $(Me_3Si)_2O$. However, apart from bistrimethylsilyl oxide, there are only small differences (13—37 cm.$^{-1}$) in the $\Delta\nu$ values for any one phenol with the various ethers, showing that the hydrogen bonds are of closely similar strengths. The contributions of the bond strength term in the free energy of association are therefore nearly constant and the considerable variations in K must arise from alteration in the entropy term, the changes in the shapes of the acceptor molecules playing a decisive part in determining the number of effective collisions which lead to association. Some part of the low K values found for the bistrimethylsilyl oxide is, of course, due to the weaker hydrogen bond, but even here entropy effects may be dominant.

A similar effect is found on passing down the columns of Table 3. The nature of the ether is now constant and the complexity of the phenol increases. In any single ether, the $\Delta\nu$ values show that phenol and its monoalkyl derivatives form hydrogen bonds of very similar strengths. Despite this, the K values change greatly as alkyl groups are introduced. Some part of the lowering of the K values found for the 2,6-dialkylphenols must be attributed to their lower acidity, but the changes are too great to be due to this alone and entropy changes must play a major part.

As expected, the incidence of entropy effects amongst the various phenols becomes more and more apparent as the complexity of the ethers is also increased. Thus the K value of phenol changes by a factor of 2·7 on passing from tetrahydrofuran to di-t-butyl ether, but the corresponding value for 2,6-di-isopropylphenol is a factor of 9. The impact of these effects in terms of the relative heights of the free and the associated peaks is very marked, and a few typical examples are illustrated in the Figure. The differences are unmistakable and could well form the basis of diagnostic techniques for the identification of substitution patterns in phenols and possibly in more complex molecules such as the sterols and triterpenes.

The Monomeric Hydroxyl Frequencies.—The values in Table 1 confirm the findings of Puttnam,[2] von Dohlen,[12] and Goddu [13] that there are two monomeric hydroxyl frequencies in some cases. One of these is at the normal value for alkylphenols, and the other is about 40 cm.$^{-1}$ higher. 5-Methyl-2-t-butylphenol, for example, shows bands at 3608s and 3647w cm.$^{-1}$, and *o*-t-butylphenol behaves similarly. Only the higher frequency absorption is shown by 2,6-di-t-butylphenol. This must indicate some steric interaction between the t-butyl and the hydroxyl group when the latter is turned towards the former. For example, the hydroxyl group might be twisted out of the plane of the ring in the *cis*-configuration, as previously suggested and since discounted by Puttnam.[2] However, in view of the high intensity of the hydroxyl band of 2,6-di-t-butylphenol, it is perhaps more likely that there is a small opening out of the C–O–H angle whereby the coplanarity of these bonds with the ring is retained.

Conclusions.—These results confirm the view that " physical " steric hindrance plays a part in preventing or weakening the association of 2,6-di-t-butylphenol with many solvents, and show that similar effects probably occur with other 2,6-dialkylphenols dissolved in

[12] Von Dohlen, personal communication.
[13] Goddu, *J. Amer. Chem. Soc.*, 1960, **82**, 4533.

bistrimethylsilyl oxide. There is also a slight weakening of the hydrogen bonds formed when some alkylphenols associate with di-t-butyl ether. These effects also appear to play a part in preventing cyclic polymeric association in *o*-t-butylphenol and in all the 2,6-dialkylphenols, although dimerisation occurs normally.

In all the other systems studied, variations in the sizes of alkyl groups on the donor or acceptor do not prevent the formation of hydrogen bonds of normal strength but do produce alterations in the equilibrium coefficients. This is attributed to a change in the proportion of collisions which are fruitful in leading to hydrogen-bond formation (entropy effects) and is not associated with any weakening of the bond once formed. This technique provides a simple method whereby entropy effects of this type can be compared, and it would seem that they are surprisingly large. Similar entropy effects would be expected to play an important part in the reaction kinetics of these materials, and some correlation should exist between the two, particularly in reactions involving a transition state formed through a hydrogen bond. There is also a reasonable parallel between the K values given above and the relative amounts of substituted phenols absorbed on charcoal from hexane solution, as reported by Wheeler and Lacey.[14]

The fact that the hydrogen atoms of many of these phenols are able to form normal associations not affected by " physical " steric hindrance does not, of course, imply that they can equally readily be replaced at the same point in space by larger groups. Steric hindrance effects are, therefore, to be expected in many of the reactions of compounds of this series despite the fact that proton donation can usually occur normally.

Part of this work was carried out during the tenure by one of us (G. E.) of a Vacation Consultancy of the Ministry of Aviation. Thanks are offered to Mrs. F. Lawrie and Mrs. S. Dingley for assistance with the experimental work and to Drs. J. C. D. Brand and C. J. W. Brooks for helpful discussions.

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[*Received, May 1st,* 1961.]

[14] Wheeler and Lacey, *Canad. J. Chem.*, 1959, 1235.

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940. 2-*Hydroxy-œstrogens. Part II.* Synthesis of* 2,3-*Dihydroxy-œstra*-1,3,5(10)-*trien*-17-*one and Œstra*-1,3,5(10)-*triene*-2,3,16α,17β-*tetraol.*

By P. Narasimha Rao and Leonard R. Axelrod.

A convenient new method is described for the synthesis of the 2-hydroxy-derivatives named in the title from œstra-1,3,5(10)-triene-2,3,17β-triol.

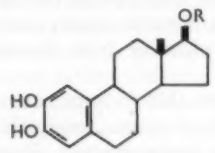
Earlier [1] we reported the synthesis of œstra-1,3,5(10)-triene-2,3,17β-triol (2-hydroxy-œstradiol-17β) from 19-nortestosterone and showed [2] that this triol-17β is converted *in vivo* into 2-methoxyœstrone, with significant quantities of other phenolic steroid metabolites. Presumptive evidence was obtained for the presence of 2,3-dihydroxyœstra-1,3,5(10)-trien-17-one (2-hydroxyœstrone) and -1,3,5(10)-triene-2,3,16α,17β-tetraol (2-hydroxy-œstriol) among these metabolites. However, to substantiate these findings it was necessary to synthesise authentic samples and we now report a practical and convenient

* Part I, *Tetrahedron*, 1960, **10**, 144.

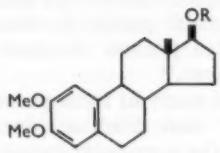
[1] Rao and Axelrod, *Chem. and Ind.*, 1959, p. 1454; *Tetrahedron*, 1960, **10**, 144.
[2] Axelrod, Rao, and Goldzieher, *Arch. Biochem. Biophys.*, 1960, **87**, 152.

method for preparing these two compounds from the 2,3,17β-triol. Other syntheses, by a different route, have been recently reported.[3,4]

17β-Acetoxy-œstra-1,3,5(10)-triene-2,3-diol (Ia), an intermediate in our earlier synthesis[1] of the triol, with methyl sulphate and anhydrous potassium carbonate in boiling acetone gave 17β-acetoxy-2,3-dimethoxyœstra-1,3,5(10)-triene (IIa) in excellent yield. Alkaline hydrolysis then gave 2,3-dimethoxyœstra-1,3,5(10)-triene-17β-ol (IIb), which was also obtained in high yield by direct methylation of the triol[1] (Ib) as above. Oxidation of the 17β-alcohol (IIb) with 8N-chromic acid[5] gave rather low yields of 2,3-dimethoxyœstra-1,3,5(10)-trien-17-one (IIIa), besides other unidentifiable oxidation products, but Oppenauer oxidation gave consistently high yields of this ketone. Compound (IIIa) was then smoothly demethylated by pyridine hydrochloride at 200°, to give 2,3-dihydroxyœstra-1,3,5(10)-trien-17-one (IIIb) in excellent yield.



(I) a: R = Ac
b: R = H



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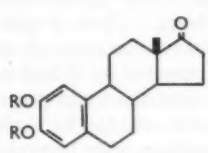
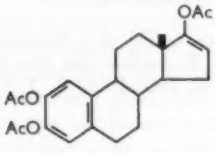
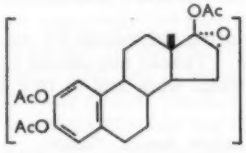


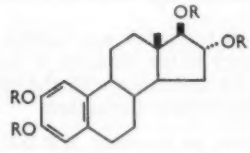
(III) a: R = Me. b: R = H
c: R = Ac



(IV)



(V)



(VI) a: R = H. b: R = Ac

The tetraol (VIa) was thence synthesised by the method of Leeds, Fukushima, and Gallagher.[6] The derived diacetate (IIIc) with isopropenyl acetate in the presence of a catalytic amount of toluene-*p*-sulphonic acid monohydrate gave 2,3,17-triacetoxyœstra-1,3,5(10),16-tetraene (IV) in satisfactory yield. This enol acetate with perbenzoic acid gave the epoxy-acetate (V), which was not isolated but was directly reduced with lithium aluminium hydride[6] in tetrahydrofuran to œstra-1,3,5(10)-triene-2,3,16α,17β-tetraol (VIa) in good yield.

TABLE 1.

Molecular rotation differences between œstrogens and 2-hydroxy-œstrogens.

Compound	$[M]_D$		$[M_D]$ 2-Hydroxy-deriv.	$\Delta[M]_D$ (2-OH)
Œstrone	+433°[a]		+477°[d]	+44°
Œstradiol-17β	+215[b]	(MeOH)	+267[e]	+52
Œstriol	+196[c]	(2·5-MeOH)	+307[d]	+111

[a] Fieser and Fieser, "Steroids," Reinhold Publ. Corp., New York, 1959, p. 463. [b] *Op. cit.*, p. 466. [c] *Op. cit.*, p. 477. [d] This paper. [e] Rao and Axelrod, *Chem. and Ind.*, 1959, 1454; *Tetrahedron*, 1960, **10**, 144.

The correctness of structure (VIa) was supported by a comparison of the molecular rotatory differences of 2-hydroxy-œstrogens shown in Table 1. Further, the ultraviolet absorption maximum at 288 mμ was typical of 2-hydroxy-œstrogens.[3,4] The infrared

[3] Fishman, Tomasz, and Lehman, *J. Org. Chem.*, 1960, **25**, 585.
[4] Coombs, *Nature*, 1960, **188**, 317.
[5] Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, p. 39; Bowers, Halsall, Jones, and Lemin, *J.*, 1953, p. 2548; Djerassi, Engel, and Bowers, *J. Org. Chem.*, 1956, **21**, 1547.
[6] Leeds, Fuhushima, and Gallagher, *J. Amer. Chem. Soc.*, 1954, **76**, 2943.

TABLE 2.

Molecular rotation data of 2-hydroxy-œstrogen acetates.

Compound	$[M]_D$	$\Delta[M]_D$ (2-OAc)
2,3-Diacetoxyœstra-1,3,5(10)-trien-17-one	+467° [a]	+12° [d]
3-Acetoxyœstra-1,3,5(10)-trien-17-one	+455° [b]	
2,3,17β-Triacetoxyœstra-1,3,5(10)-triene	+217° [c]	+71
3,17β-Diacetoxyœstra-1,3,5(10)-triene	+146° [b]	
2,3,16α,17β-Tetra-acetoxyœstra-1,3,5(10)-triene	−19° [a]	+63
3,16α,17β-Triacetoxyœstra-1,3,5(10)-triene	−82° [b]	

[a] This paper. [b] Determined in our laboratories. [c] Rao and Axelrod, *Chem. and Ind.*, 1959, 1454; *Tetrahedron*, 1960, **10**, 144. [d] Although the reported value for œstrone 3-acetate (Velliuz and Muller, U.S.P. 2,773,886, $[M]_D$ + 400°) yields a 2-acetoxy-contribution more in agreement ($\Delta[M]_D$ +67°) with the other acetates reported in this paper, an analytical sample of 3-acetoxyœstrone gave a higher value of the molecular rotation in our hands.

spectrum included peaks similar to those for the other 2-hydroxy-œstrogens between 1650 and 1400 cm.$^{-1}$ (aromatic ring).[7] Unequivocal proof was provided by preparing the formation of a tetra-acetate (VIb). The molecular rotatory differences for the acetates of 2-hydroxy-œstrogens are shown in Table 2 and are in good agreement within experimental error. As expected, the tetraol (VIa) was more polar than œstriol and other 2-hydroxy-œstrogens, as indicated by paper partition chromatography. The physical constants of our compound (VIa) are in agreement with those reported by Coombs,[4] except that we obtained a higher value of $[\alpha]_D$.

EXPERIMENTAL

Microanalyses were performed by Messrs. Micro-Tech Laboratories, Skokie, Illinois, U.S.A. M. p.s were determined on samples dried under a high vacuum at 60° for 24 hr. Ultraviolet absorption spectra were determined for methanol solutions with a Cary recording spectrophotometer (model 11 MS). The infrared spectra were determined for potassium bromide discs on a Perkin-Elmer (model 21) infrared spectrometer. Rotations were determined for chloroform solutions unless otherwise stated, with a Zeiss–Winkel polarimeter. Merck " Reagent grade " aluminium oxide, " Suitable for chromatographic adsorption," treated with ethyl acetate and then activated to give Brockmann activity II—III, was used in chromatography. Light petroleum used was that of Mallinckrodt " Analytical Reagent grade " and b. p. 30—60°.

17β-*Acetoxy*-2,3-*dimethoxyœstra*-1,3,5(10)-*triene* (IIa).—17β-Acetoxy-1,3,5(10)-triene-2,3-diol (Ia) (4 g.) was heated in anhydrous acetone (430 ml.) with anhydrous potassium carbonate (123 g.) and dimethyl sulphate (43 ml.) for 6 hr. (ferric chloride–potassium ferricyanide test [8] negative), then the excess of methyl sulphate was decomposed by water (20 ml.) and warming on a water bath. Most of the acetone was evaporated under a vacuum at 40° and the residue was treated with water (500 ml.) and then extracted with ethyl acetate. The extract was washed with water until neutral, then dried (Na_2SO_4) and evaporated. The residue crystallised from methanol to give (3·6 g., 83%) 17β-acetoxy-2,3-dimethoxyœstra-1,3,5(10)-triene, m. p. 180—181°, $[\alpha]_D^{29}$ +59° (*c* 0·51), $\lambda_{max.}$ 282 mμ (ε 4843), $\lambda_{min.}$ 252 mμ (ε 1132), $\nu_{max.}$ 1726, 1608, and 1512 cm.$^{-1}$ (Found: C, 73·6; H, 8·2. Calc. for $C_{22}H_{30}O_4$: C, 73·7; H, 8·4%) (lit.,[3] m. p. 179—182°, $[\alpha]_D^{27}$ +53°).

2,3-*Dimethoxyœstra*-1,3,5(10)-*trien*-17β-*ol* (IIb).—Compound (IIa) (3·4 g.) was heated in 5% methanolic potassium hydroxide (300 ml.) for 2 hr. The usual working up gave 2,3-dimethoxyœstra-1,3,5(10)-trien-17β-ol (2·9 g.) that, crystallised from acetone–light petroleum, had m. p. 130—132°, $[\alpha]_D^{23·5}$ +82° (*c* 0·78), $\lambda_{max.}$ 285 mμ (ε 3828), $\lambda_{min.}$ 255 mμ (ε 561), $\nu_{max.}$ 3500, 1613, and 1515 cm.$^{-1}$ (Found: C, 75·9; H, 9·0. Calc. for $C_{20}H_{28}O_3$: C, 75·9; H, 8·9%) (lit.,[3] m. p. 131—133°, $[\alpha]_D^{27}$ +85°).

Compound (IIb) was also obtained by a similar methylation of the triol (Ib), as above, in 80% yield and crystallised from acetone–light petroleum (m. p. and mixed m. p. 130—132°; correct infrared spectrum).

[7] Bellamy, " The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, 1959, p. 64.

[8] Barton, Evans, and Gardner, *Nature*, 1952, **170**, 249.

2,3-*Dimethoxyœstra*-1,3,5(10)-*trien*-17-*one* (IIIa).—(*a*) To a cold solution (10—15°) of the triol (IIb) (290 mg.) in acetone (30 ml.; distilled from permanganate) in an atmosphere of nitrogen, 8N-chromium trioxide [5] was added dropwise till the reddish-brown colour persisted. After an additional 2 minutes' stirring, the mixture was diluted with water (500 ml.) and extracted with ethyl acetate. The extract was washed with water, saturated sodium hydrogen carbonate solution, and with water until neutral. The product (287 mg.) was then chromatographed on alumina (8·5 g.). Elution with light petroleum–benzene (1 : 1) gave 2,3-dimethoxyœstra-1,3,5(10)-trien-17-one (115 mg., 39%) which, crystallised from acetone, had m. p. 170—172°, $[\alpha]_D^{24}$ +161° (*c* 0·63), $\lambda_{max.}$ 285 mμ (ε 4024), $\lambda_{min.}$ 255 mμ (ε 753), $\nu_{max.}$ 1720, 1605, and 1515 cm.$^{-1}$ (Found: C, 76·0; H, 8·2. Calc. for $C_{20}H_{26}O_3$: C, 76·4; H, 8·3%) (lit.,[3] m. p. 173—176°).

Further elution of the column with benzene and benzene–ether (8 : 2) gave a product (160 mg.) which resisted crystallisation, $\nu_{max.}$ 1730, 1710, and 1665 cm.$^{-1}$ (C=O), that was not further investigated.

(*b*) To the triol (IIb) (2·89 g.) in dry toluene (600 ml.) cyclohexanone (28 ml.) and aluminium isopropoxide (6 g.) were added, and the whole heated under reflux for 4 hr., then washed with 10% sulphuric acid, water, saturated hydrogen carbonate solution, and water until neutral. Toluene and most of the excess of cyclohexanone were removed under reduced pressure and the residue was chromatographed on alumina (100 g.). The ketone (IIIa), m. p. 170—172° (1·9 g., 68%), eluted with light petroleum–benzene (1 : 1), was identical (mixed m. p.; infrared spectrum) with that obtained as in (*a*). Further elution of the column with benzene and benzene–ether (1 : 1) gave unoxidised product (IIb) (700 mg.), m. p. 129—131°.

2,3-*Dihydroxyœstra*-1,3,5(10)-*trien*-17-*one* (IIIb).—The ether (IIIa) (2·5 g.) and freshly distilled pyridine hydrochloride (5 g.) were heated for 1 hr. at 200° under nitrogen, then diluted with water and the precipitated 2,3-dihydroyxœstra-1,3,5(10)-trien-17-one (IIIb) was filtered off. It (2·2 g., 90%) crystallised from acetone–light petroleum and had m. p. 194—195°, $[\alpha]_D^{24}$ +166° (*c* 0·5 in EtOH), $\lambda_{max.}$ 288 mμ (ε 3796), $\lambda_{min.}$ 254 mμ (ε 366), $\nu_{max.}$ 3370b, 1722, 1610, and 1515 cm.$^{-1}$ (Found: C, 75·2; H, 7·9. Calc. for $C_{18}H_{22}O_3$: C, 75·5; H, 7·8%) (cf. refs. 3 and 4).

The 2,3-diacetate was prepared with pyridine and acetic anhydride in the cold and crystallised from methanol in needles, m. p. 164—166°, $[\alpha]_D^{29}$ +126° (*c* 0·75), $\lambda_{max.}$ 278 (ε 1390), 271 mμ (ε 1390), $\lambda_{min.}$ 274 (ε 1269), 249 mμ (ε 315), $\nu_{max.}$ 1770, 1730, and 1505 cm.$^{-1}$ (Found: C, 71·2; H, 7·2. Calc. for $C_{22}H_{26}O_5$: C, 71·3; H, 7·1%) (lit.,[4] m. p. 170—171°).

2,3,17-*Triacetoxyœstra*-1,3,5(10),16-*tetraene* (IV).—To a solution of diacetate (IIIc) (1·95 g.) in isopropenyl acetate (75 ml.), toluene-*p*-sulphonic acid monohydrate (700 mg.) was added and the whole was refluxed for 15 min. The isopropenyl acetate was then distilled off during 6 hr., being replaced by fresh reagent to maintain the volume constant. The mixture was then cooled and diluted with ether. The ether solution was washed with ice-cold 5% sodium hydrogen carbonate solution and water until neutral, dried, and evaporated. The residue was chromatographed on a short column of alumina (70 g.). The combined material (775 mg., 35%), m. p. 160—162°, eluted with light petroleum–benzene (1 : 1) and benzene, crystallised from acetone–light petroleum, giving 2,3,17-*triacetoxyœstra*-1,3,5(10),17-*tetraene*, m. p. 166—168°, $[\alpha]_D^{26}$ +82° (*c* 0·51), $\lambda_{max.}$ 273 (ε 1432), 278 mμ (ε 1469), $\lambda_{min.}$ 276 (ε 1344), 253 mμ (ε 828), $\nu_{max.}$ 1765, 1630, 1505, and 1375 cm.$^{-1}$ (Found: C, 69·8; H, 6·8. $C_{24}H_{28}O_6$ requires C, 69·9; H, 6·8%).

Œstra-1,3,5(10)-*triene*-2,3,16α,17β-*tetraol* (IVa).—To a solution of the enol acetate (IV) (1 g., 0·0025 mole) in benzene (20 ml.), a 0·33M-solution (18·8 ml.) of perbenzoic acid in chloroform was added and the whole was set aside for 20 hr., then diluted with benzene (100 ml.) and washed with 2% ice-cold sodium hydroxide solution and water until neutral.

The residue (1 g.) obtained on evaporation was added in dry tetrahydrofuran (100 ml.) with stirring to lithium aluminium hydride (1·25 g.) in tetrahydrofuran (50 ml.) in 15 min., then the mixture was heated under reflux for 2 hr. The excess of reagent was destroyed by ethyl acetate. The hydride complex was decomposed with 5% ice-cold hydrochloric acid and then extracted with a large quantity of ethyl acetate. The ethyl acetate solution was washed with water, 5% sodium hydrogen carbonate solution, and water until neutral. After drying and evaporation the residue (700 mg.) was a gum which, crystallised from dilute methanol, had m. p. 253—256° (decomp.). Two additional crystallisations from 80% methanol and one finally from absolute methanol gave the pure tetraol with constant m. p. 262—263° (vac.), $[\alpha]_D^{29}$ +80° (*c* 0·79 in

MeOH), $\lambda_{max.}$ 288 mμ (ε 3968), $\lambda_{min.}$ 253 mμ (ε 599), $\nu_{max.}$ 3440b, 1613, 1515, and 1450 cm.$^{-1}$. The material, despite drying at 60° in a high vacuum, retained solvent tenaciously (Found: C, 64·2; H, 8·4. Calc. for $C_{18}H_{24}O_4,2\frac{1}{2}CH_3{\cdot}OH$: C, 64·0; H, 8·8%) (cf. ref. 4).

The tetraol (300 mg.), pyridine (10 ml.), and acetic anhydride (6 ml.) at 70° (3 hr.) gave the *tetra-acetate*, needles (from aqueous methanol), m. p. 96—100°, $[\alpha]_D^{25}$ −4° (*c* 0·5), $\lambda_{max.}$ 268 (ε 1815), 277 mμ (ε 1579), $\lambda_{min.}$ 257 (ε 795), 275 mμ (ε 1517), $\nu_{max.}$ 1773, 1743, 1505, and 1375 cm.$^{-1}$ (Found: C, 65·7; H, 6·7. $C_{26}H_{32}O_8$ requires C, 66·0; H, 6·8%).

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941. *Controlled-potential Electrolysis. Part VI.*[1] *Reductions of 2,2-Dinitropropane.*

By Masaichiro Masui and Hiroteru Sayo.

The reduction processes of 2,2-dinitropropane have been studied by controlled-potential electrolysis. In alkaline solution the two-electron reduction to the *aci*-form of 2-nitropropane and nitrite was established by isolation of 2-nitro-2-nitrosopropane. In acid solution the reduction at the plateau potential of the first wave yielded acetoxime and nitrous acid by a four-electron reduction; the uptake at the second wave was 10·6-electrons, the reduction giving ammonia, hydroxylamine, 2-hydroxylaminopropane, and acetoxime. On these bases the reduction processes and the polarograms of 2,2-dinitropropane are discussed.

Only Stock[2] has studied the polarographic reduction of 2,2-dinitropropane. He used a small-scale, controlled-potential, electrolytic method for an alkaline solution and found that the reduction wave was due to the reduction to the *aci*-form of 2-nitropropane and nitrite ion, but he merely deduced the mechanisms of the reduction waves in acid solution and gave no evidence in support.

As part of our study of controlled-potential electrolysis of nitro-compounds we applied the method to 2,2-dinitropropane on a fairly large scale and have clarified the reduction processes by isolating the products. Only the result obtained in alkaline solution has agreed with Stock's work.

Table 1.

Half-wave potentials and diffusion current constants of 2,2-dinitropropane in buffer solutions containing 10% of ethanol.

pH	2·0 *	4·0 *	6·0	8·0	10·0	12·0
$\pi_{\frac{1}{2}}$ (v)	−0·348	−0·465	−0·488	−0·496	−0·486	−0·499
$i_d/cm^{\frac{1}{2}}t^{\frac{1}{2}}$	4·35	3·87	3·00	3·16	2·94	2·84

Polarography.†—Because of the low solubility of 2,2-dinitropropane in water it was necessary to use ethanol for the more concentrated solutions required. The polarographic behaviour of 2,2-dinitropropane in 10% ethanolic buffer solutions were, therefore, first investigated. The results (Table 1) were almost the same as Stock's, except that the poorly defined second wave (marked *) was overlapped by the reduction wave of hydrogen ion.

Controlled-potential Electrolysis in Alkaline Solution.—Stock's results for alkaline

† All voltages are measured against the saturated calomel electrode.

[1] Part V, *J. Pharm. Soc. Japan*, 1960, **80**, 1256.
[2] Stock, *J.*, 1957, 4532.

solution were confirmed in our experiments on a larger scale. The electrolysed solutions became blue when acidified and the coloured substance was identified as 2-nitro-2-nitrosopropane by isolation in crystalline form. The compound is derived according to reaction (1) which is used as a test for secondary nitroparaffins.[2]

$$RR'C{=}NO{\cdot}O^- + NO_2^- + 2H^+ \longrightarrow RR'C(NO){\cdot}NO_2 + H_2O \quad . . . . . (1)$$

On the other hand, the presence of excess of sodium azide and slow acidification prevented the coloration of the solution, which only showed a single reduction wave of 2-nitropropane.[3] Stock's reaction (2) is thus confirmed.

$$Me_2C(NO_2)_2 + 2e \longrightarrow Me_2C{=}NO{\cdot}O^- + NO_2^- \quad . . . . . (2)$$

Controlled-potential Electrolysis at a Plateau Potential of the First Wave in Acid Solution.—Electrolysis at −0·55 v in buffer solutions of pH 2 was slow and consumed four electrons per molecule (Table 2).

The electrolysed solution gave a positive test for nitrite and yielded a yellow precipitate with 2,4-dinitrophenylhydrazine. These solutions did not reduce Fehling's solution until after hydrolysis with boiling dilute sulphuric acid. Neutralisation of the electrolysed solution, removal of the ethanol, and extraction with ether afforded acetoxime, whence two reduction processes, (3) and (4), are inferred.

According to eqn. (3), a four-electron reduction proceeds in one step at the electrode surface, and the product is hydrolysed to acetoxime and nitrous acid. By eqn. (4), the first step is a two-electron reduction to 2-nitropropane and nitrite (as in basic media) then reaction with hydrogen ion to form 2-nitro-2-nitrosopropane, which is reduced in the second step by a two-electron process. If a four-electron reduction, as in eqn. (3), took place, the limiting current of the first wave should be about twice as high in acid as in

$$Me_2C(NO_2)_2 \xrightarrow{+4e+4H^+} Me_2C(NO_2){\cdot}NH{\cdot}OH \longrightarrow Me_2C{:}N{\cdot}OH + HNO_2 \quad . . . (3)$$

$$Me_2C(NO_2)_2 \xrightarrow{+2e} Me_2C{:}NO_2^- + NO_2^- \xrightarrow{+2H^+} Me_2C(NO_2){\cdot}NO \xrightarrow{+2e+2H^+} Me_2C{:}N{\cdot}OH + HNO_2 \quad . (4)$$

alkaline solution and also be diffusion-controlled. But the height of the former is only 1·4 times that of the latter and the effect of mercury-column height on the limiting current does not imply diffusion-control (Table 3).

With reduction in the presence of sulphamic acid (to decompose nitrous acid) the uptake fell to about 3 electrons per molecule; thus some of the nitrous acid produced is consumed in the reduction. Nitrous acid is not reducible at this potential, so that if the reduction proceeds according to eqn. (3), the decomposition of nitrous acid should cause no change in current requirements.

TABLE 2.

Reduction of 2,2-dinitropropane at −0·55 v at pH 2.

Taken (mg.)	203·0	251·1	369·7
Coulombs reqd. Found	572	710	1062
n, found	3·92	3·93	3·99

According to eqn. (4) the intermediate, 2-nitro-2-nitrosopropane, should be reduced under this condition as produced, because its half-wave potential is −0·05 v at pH 2. This was proved by the reduction of 2-nitro-2-nitrosopropane, prepared according to Meyer,[3] under the same conditions; acetoxime and nitrous acid were obtained by a two-electron reduction. During electrolysis the solution became blue—the colour of nitro-nitroso-compounds—and again colourless towards the end of the reduction. The time required to complete reduction was always considerably greater than for alkaline solution. These results indicate that the reduction in acid solution is expressed by eqn. (4).

[3] Meyer, *Annalen*, 1875, **175**, 120.

TABLE 3.

Effect of mercury-column height on limiting current of 2,2-dinitropropane.

At pH2	h (cm.)	40	50	60	70
	i_l(μA)	6·45	7·15	7·80	8·40
	$i_l h^{-\frac{1}{2}}$	1·020	1·011	1·007	1·004
In 0·1N-NaOH	i_l(μA)	4·20	4·70	5·15	5·55
	$i_l h^{-\frac{1}{2}}$	0·664	0·665	0·665	0·663

Controlled-potential Electrolysis at a Potential beyond the Second Wave in Acid Solution.—2,2-Dinitropropane consumed about ten electrons per molecule in electrolysis at pH 2 at −1·15 v (see Table 4).

The reduction mixture, when made alkaline and distilled, gave ammonia and with sufficient boiling sulphuric acid reduced Fe^{3+} to Fe^{2+}; however, it gave only a slight precipitate with 2,4-dinitrophenylhydrazine. Nitrous acid is reduced under these conditions to a mixture of hydroxylamine and ammonia in an approximately 4·6-electron process. There are therefore two reduction processes to be discussed: (*a*) the nitrous acid produced by the first step is reduced before it reacts with 2-nitropropane so that 2-nitro-2-nitrosopropane is not produced [eqn. (5)], and (*b*) 2-nitro-2-nitrosopropane is produced by reaction between 2-nitropropane, nitrite, and hydrogen ion, as shown in eqn. (4), and this is reduced first to acetoxime and nitrous acid and then to hydroxylamine and ammonia [eqn. (6)].

Calculations for eqns. (5) and (6) give 10·6 and 8·6 electrons per molecule of 2,2-dinitropropane respectively,* since acetoxime was proved experimentally not to be reduced at this potential. Though the amounts of final products, 2-hydroxyaminopropane, acetoxime, hydroxylamine, and ammonia, could not be estimated accurately, rough

TABLE 4.

Reduction of 2,2-dinitropropane at −1.15 v at pH 2.

Taken (mg.)	39·0	40·3	44·7
Coulombs, reqd. Found	280	294	332
n, found	9·98	10·14	10·31

calculation † for the actual reduction show that only a quarter of the original compound is reduced according to eqn. (6), whilst the very low yield of acetoxime indicates that the larger part is reduced according to eqn. (5).

Interpretation of Polarograms in Acid Solutions.—Stock has stated that the increased height of the first wave in acid solution is due to either the reduction of un-ionized *aci*-form or the catalytic discharge of hydrogen ions, and that the second wave is due to the

$$Me_2C(NO_2)_2 \xrightarrow{+2e} Me_2C{:}NO_2^- + NO_2^- \xrightarrow{+2H^+} Me_2CH{\cdot}NO_2 + HNO_2 \longrightarrow Me_2CH{\cdot}NH{\cdot}OH + NH_2{\cdot}OH + NH_3 \quad (5)$$

reduction of nitrous acid to nitrogen, requiring 3-electrons. However, the results of our controlled-potential electrolysis lead to a different interpretation. They indicate that the first wave includes a 2-electron reduction of 2,2-dinitropropane to the *aci*-nitropropane and nitrite ion which form the nitro-nitroso-compound, some of which is also reduced. This is why the height of the first wave in acid solution is much greater than that in alkaline solution (see Table 1). Also the second wave cannot be attributed to a

$$Me_2C(NO_2)_2 \xrightarrow{+2e} Me_2C{=}NO_2^- + NO_2^- \xrightarrow{+2H^+} Me_2C(NO_2){\cdot}NO \xrightarrow{+2e+2H^+} Me_2C{:}N{\cdot}OH + HNO_2 \longrightarrow Me_2C{=}N{\cdot}OH + NH_2{\cdot}OH + NH_3 \quad (6)$$

* 10·6 e = 2 e (2,2-dinitropropane ⟶ 2-nitropropane $+NO_2^-$) + 4 e (2-nitropropane ⟶ 2-hydroxyaminopropane) +4·6 e (experimental value for $HNO_2 \longrightarrow NH_2{\cdot}OH + NH_3$):
8·6 e = 2 e (2,2-dinitropropane ⟶ 2-nitropropane $+NO_2^-$) + 2 e (2-nitro-2-nitrosopropane ⟶ acetoxime) +4·6 e (experimental value for $HNO_2 \longrightarrow NH_2{\cdot}OH + NH_3$).

† From the eqn. $10{\cdot}6a + 8{\cdot}6(1 - a) = 10{\cdot}1$, we obtain $a = 0{\cdot}75$, where a is the proportion following eqn. (5), and 10·1 is the mean value derived from Table 4.

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simple reduction of nitrous acid to nitrogen, but is due to a combination of reductions of (*a*) nitrous acid to hydroxylamine and ammonia, (*b*) nitro-nitroso-compound formed from the *aci*-form of 2-nitropropane, nitrous acid and protons, and (*c*) nitro-form of 2-nitropropane transformed from its *aci*-form. The rates of formation of nitro-nitroso-compound and of transformation of *aci*-form to nitro-form are rather slow; therefore the diffusion of products into solution from the surface of the electrode makes the height of the second wave smaller than would be expected from consideration of electron consumption, about 10, as measured in controlled-potential electrolysis in which all reducible substances are reduced.

Experimental

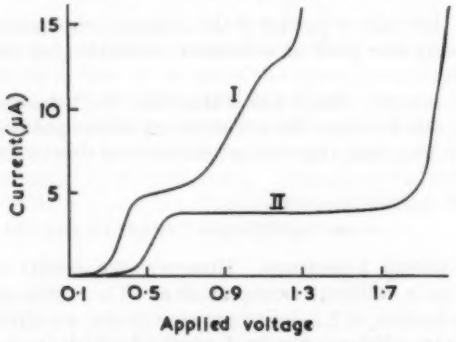
Apparatus.—Current–voltage curves were obtained with Yanagimoto type PEL-3 and GR-3 galvarecorder in a constant-temperature bath at 25° (±0·1°). The capillary characteristics were $m = 0{\cdot}937$ mg. sec.$^{-1}$, $t = 3{\cdot}68$ sec., $m^{\frac{2}{3}} t^{\frac{1}{6}} = 1{\cdot}194$. The macro-electrolyses were carried out by using a Yanagimoto potentiostat type VE, model 3. The electrolysis cell used was of Lingane–Jones type, with a mercury cathode surface of about 50 cm.^{2} The total quantity of electricity passed was measured by graphical integration of the plots of current against time.

Reagents.—2,2-Dinitropropane was prepared by chromic acid oxidation [4] of 2-nitro-2-nitrosopropane, which was prepared from 2-nitropropane and sodium nitrite. After purification by distillation it had b. p. 70°/10 mm., m. p. 53°.

Buffer solutions used for polarographic analysis were of Britton–Robinson type containing 0·1M-potassium chloride as additional supporting electrolyte. pH values were measured by a Toa Dempa glass electrode pH meter HM-5.

Oxygen was removed by a stream of nitrogen.

Reduction of 2,2-Dinitropropane in 0·1N-Sodium Hydroxide.—The compound (400 mg.) was reduced at −0·75 v in a mixture of 0·1N-sodium hydroxide (360 ml.), potassium chloride (1·5 g.), and ethanol (40 ml.). The electrolysed solution was acidified with dilute hydrochloric acid and extracted with ether, and the extract dried (Na_2SO_4). Evaporation gave a residue which was washed with cold ether to give 2-nitro-2-nitrosopropane, m. p. 76° (decomp. in sealed tube) (Found: C, 30·9; H, 5·4. Calc. for $C_3H_6N_2O_3$: C, 30·5; H, 5·1%).



Polarograms of 10^{-3}M-2,2-dinitropropane.
Curve I, pH 2·0; curve II, pH 12·0.

Reduction of 2,2-Dinitropropane at pH 2.—(*a*) This compound (200 mg.) was reduced at −0·55 v in a mixture of 0·1M-phosphoric acid (270 ml.), adjusted to pH 2 with sodium hydroxide, potassium chloride (1·1 g.), and ethanol (30 ml.). Products from two runs were combined and neutralized with 10% sodium hydroxide. Ethanol was distilled off and the residue was extracted with ether after being saturated with sodium chloride. Removal of ether and storage of the residue in a vacuum desiccator overnight gave acetoxime, m. p. 60° (2,4-dinitrophenylhydrazone, m. p. 128°).

(*b*) The compound (40 mg.) was reduced at −1·15 v as described above, but nitrogen was introduced on the surface of the solution to prevent loss of nitrous acid from the solution.

Reduction of Nitrous acid in a Solution at pH 2.—Sodium nitrite (23·5 mg.) was reduced

[4] Born, *Ber.*, 1896, **29**, 93.

as described in (*b*) above. From the reduction mixture hydroxylamine (64%) was evaluated potentiometrically by use of ferric iron and potassium dichromate, and ammonia (33%) was determined by titration.

We thank Professor Kiyoshi Takiura for his interest.

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942. *Phosphonitrilic Derivatives. Part VII.*[1] *The Crystal Structure of Tetrameric Phosphonitrilic Fluoride.*

By H. McD. McGEACHIN and F. R. TROMANS.

The *X*-ray analysis of crystalline $(PNF_2)_4$ shows that the P–N ring is planar and that the molecule has only slight deviations from $4/mmm$ (D_{4h}) symmetry. These deviations are ascribed to close approaches of neighbouring molecules. The P–N bond lengths are equal and short (1·51 ± 0·02 Å). The P–F bond lengths are also 1·51 ± 0·02 Å and values of 147·2° ± 1·4°, 122·7° ± 1·0° and 99·9° ± 1·0° are found for the angles $\widehat{PNP}$, $\widehat{NPN}$, and $\widehat{FPF}$, respectively.

THIS study was undertaken to investigate the structural effects of substituting fluorine for chlorine in the phosphonitrilic halides. Ketelaar and de Vries [2] showed that the symmetry of the tetrameric chloride was $\bar{4}$ while space-group considerations indicated that that of the fluoride was $\bar{1}$. The shape of the eight-membered P–N ring thus depends on the substituents; this work reports how the bond lengths and angles are modified by the substitution of the more electronegative fluorine for chlorine.

Shortly before our work was completed, Jagodzinski and Oppermann [3] published an account of some preliminary structural work on $(PNF_2)_4$; they do not intend to continue the investigation. A brief note on our results has appeared.[4]

Crystal Data.—$(PNF_2)_4$, $M = 331{\cdot}96$, m. p. 30·4°, monoclinic, $a = 7{\cdot}40$, $b = 13{\cdot}83$, $c = 5{\cdot}16$ Å, $\beta = 109{\cdot}5°$, $U = 500$ Å^3, $D_m = 2{\cdot}22$, $Z = 2$, $D_c = 2{\cdot}20$, $F(000) = 320$, $\mu = 8{\cdot}8$ cm.$^{-1}$ Mo for radiation. Space group $P2_1/a$ (C^5_{2h}, No. 14), implied molecular symmetry $\bar{1}$, optically biaxial negative, refractive indices $\alpha = 1{\cdot}379 \pm 0{\cdot}002$, $\beta = 1{\cdot}428 \pm 0{\cdot}005$, $\gamma = 1{\cdot}463 \pm 0{\cdot}002$ (optical results from J. K. Leary). Because of the low melting point, the thermal vibrations are large and no high-order reflections are observed. The dimensions of the unit cell, determined from rotation photographs, are therefore probably less accurate than we would wish; they can be compared with Jagodzinski and Oppermann's values $a = 7{\cdot}53$, $b = 14{\cdot}0$, $c = 5{\cdot}15$ Å, $\beta = 111{\cdot}1°$.

EXPERIMENTAL

Tetrameric phosphonitrilic fluoride sublimes rapidly in air and crystal specimens must be grown in sealed capsules. Two different sets of three-dimensional intensity measurements were made. In the first (*A*), one of several single crystals grown from the melt in a Lindemann glass tube was used with copper radiation. It was impossible to control the shape of the specimen, and during exposure both size and shape changed as the crystal sublimed inside the tube. Since we had no precise knowledge of the crystal dimensions, we could not apply the anisotropic absorption corrections which were clearly desirable. At a later stage another set (*B*) of intensity measurements were made with molybdenum radiation and a spherical crystal. This was grown in a Lindemann glass sphere (0·8 mm. diam.) completely filled with the melt; cycles of partial melting and recrystallisation (controlled either by varying the

[1] Part VI, Chapman, Holmes, Paddock, and Searle, *J.*, 1961, 1825.
[2] Ketelaar and de Vries, *Rec. Trav. chim.*, 1939, **58**, 1081.
[3] Jagodzinski and Oppermann, *Z. Krist.*, 1960, **113**, 241.
[4] McGeachin and Tromans, *Chem. and Ind.*, 1960, 1131.

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TABLE 1.

Observed and calculated structure factors.

h k l	$10\|F_o\|$	$10F_c$	*h k l*	$10\|F_o\|$	$10F_c$	*h k l*	$10\|F_o\|$	$10F_c$	*h k l*	$10\|F_o\|$	$10F_c$	*h k l*	$10\|F_o\|$	$10F_c$
0 0 1	351	295	2 2 −4	90	90	3 4 −3	235	265	4 6 −3	74	−89	1 9 −2	204	203
2	382	−384	3 2 0	51	28	−4	159	−151	−4	123	134	2 9 0	154	143
3	353	377	1	335	−335	4 4 0	110	100	5 6 0	62	66	1	153	−143
5	79	−83	2	236	−254	1	94	−77	1	46	41	3	106	94
2 0 0	1248	−1210	3	72	−82	2	105	−95	−1	149	150	−2	95	−101
1	139	−167	−1	163	163	−1	112	130	−2	120	112	3 9 0	111	−96
3	239	−277	−2	290	281	−2	156	154	−3	84	77	1	116	−113
4	93	−107	−3	342	303	−3	192	199	−4	71	60	−1	147	−139
−1	442	357	4 2 0	119	140	−4	147	146	6 6 1	81	77	−2	181	−181
−2	522	487	1	72	77	5 4 1	89	−100	−1	88	−71	4 9 0	135	−128
−3	248	−224	2	79	−83	2	83	69	7 6 0	79	−65	1	65	68
−4	176	165	−1	118	−135	−1	166	174	1	154	155	3	71	−84
−5	63	87	−3	65	63	−2	113	−113	2	110	−111	−2	117	118
4 0 0	103	106	−4	72	−72	−3	95	−94	3	199	−223	5 9 0	93	90
1	199	207	5 2 1	140	−155	−4	89	88	1 7 0	192	−181	1	91	98
2	64	−43	3	88	70	6 4 0	187	−185	1	159	170	2	58	48
4	85	83	−1	93	−106	−1	178	−160	3	132	−141	−1	108	117
−1	353	−387	−2	334	−337	−3	53	−68	−2	136	134	−2	48	39
−2	276	−256	−3	130	−136	7 4 −2	100	76	2 7 1	126	−120	−3	50	−45
−3	120	−134	6 2 1	55	−57	0 5 1	153	155	3	132	135	6 9 0	54	42
−4	257	−227	−1	45	48	2	78	42	−1	178	−162	−1	61	−42
6 0 0	211	218	7 2 −2	129	160	4	103	−67	−2	277	−249	0 10 0	145	177
1	56	−53	0 3 1	450	−349	1 5 0	368	−232	−3	140	−152	1	88	83
−1	234	259	2	144	172	1	99	−86	3 7 0	396	367	1 10 0	375	358
−3	86	89	3	294	278	2	124	137	1	142	−122	1	96	96
−4	88	137	4	60	−62	3	117	82	2	87	−93	2	70	−83
0 1 1	57	−56	1 3 1	116	112	4	129	136	3	111	97	3	119	95
2	89	76	3	105	83	−2	136	−135	−2	204	−208	2 10 0	115	−110
3	111	110	−1	369	−301	−3	101	−104	−3	125	123	1	132	−162
1 1 0	397	343	2 3 0	200	−181	−4	121	−117	4 7 0	74	72	3 10 0	154	−136
1	709	−624	1	149	146	2 5 0	290	−266	1	173	184	1	146	−139
2	101	−97	3	229	−233	1	147	164	2	102	107	−1	206	219
3	117	113	−1	267	232	2	135	133	−1	140	142	−2	114	95
4	161	−172	−2	380	337	−1	140	120	−2	128	127	4 10 1	73	77
−1	823	779	−3	121	99	−2	117	162	5 7 0	106	−121	−1	63	−63
−3	136	−151	3 3 0	191	−157	−3	143	−150	1	68	59	−2	43	−55
−4	137	151	1	60	54	3 5 0	243	235	2	94	82	5 10 −1	135	−125
2 1 0	131	136	3	60	−46	1	67	63	−1	76	82	−4	90	−55
1	167	−152	−1	54	−51	−2	160	164	−2	99	88	0 11 1	235	252
2	180	−177	−2	102	109	−3	159	176	−3	108	−94	2 11 0	175	180
3	89	−102	−3	73	−37	4 5 0	220	224	6 7 0	60	−46	1	132	−150
−1	247	217	4 3 0	100	116	1	42	−36	1	63	−55	−1	271	281
−3	85	67	1	162	−203	−1	63	−58	−1	75	−69	3 11 0	116	−133
3 1 0	213	−260	2	172	−181	−2	179	−179	0 8 0	88	93	1	59	50
1	221	234	3	74	93	−3	92	100	1	374	357	4 11 0	168	−187
2	85	71	−1	306	−320	5 5 0	306	−289	2	219	217	−1	83	−82
3	141	−149	−2	156	−162	1	126	−129	3	120	−124	−3	47	−53
−1	111	−121	−3	108	108	−3	116	−97	1 8 0	59	58	5 11 0	46	45
3	86	−61	5 3 0	78	−71	−4	48	55	1	73	−81	6 11 0	80	87
0	63	−59	1	122	−130	−5	74	45	2	139	−132	0 12 1	112	−141
1	58	−76	3	55	26	6 5 0	87	−85	−1	230	−219	2	98	−76
2	97	−85	−3	60	−12	2	77	30	−3	137	132	1 12 0	187	260
−1	158	−201	6 3 2	112	109	7 5 0	78	59	2 8 0	131	145	1	58	37
−2	65	70	−1	226	231	0 6 0	288	−255	1	72	−51	−2	68	−75
−3	57	53	−3	122	−143	1	98	102	2	276	−289	2 12 0	104	−60
5 1 0	317	350	0 4 0	1248	−1095	3	120	−114	−1	258	−260	2	124	114
1	78	67	1	452	−383	1 6 0	67	−95	−3	191	204	−1	58	73
2	69	−61	2	192	−183	1	298	−278	3 8 0	63	−59	3 12 0	102	−113
3	62	70	3	112	−135	2	226	−212	2	158	147	−2	70	46
−3	100	117	4	53	58	3	137	−110	−1	169	166	4 12 −2	82	82
−4	75	−80	1 4 0	536	−518	4	149	14	−2	68	−48	−3	70	69
6 1 2	73	60	1	76	82	−1	296	−287	−3	114	−138	0 13 1	84	57
−1	126	163	2	253	251	−2	310	−319	4 8 0	70	−74	1 13 2	74	78
−3	132	−86	3	116	−123	2 6 0	175	179	2	119	108	−2	123	−118
7 1 0	62	−90	−1	503	495	1	119	135	−1	82	81	3 13 1	85	80
0 2 0	687	430	−2	104	101	−1	325	−289	−2	161	−177	−1	104	90
1	177	−145	−3	394	−310	−2	89	82	−3	189	−188	−2	104	107
2	103	−105	−4	71	67	−3	146	154	5 8 2	55	−57	5 13 1	64	−46
3	90	107	2 4 0	244	190	−4	165	−164	−1	46	−58	−1	83	−86
1 2 0	83	65	1	78	76	3 6 1	192	182	−2	65	45	−3	69	53
1	910	815	2	320	300	2	127	121	−3	84	75	1 14 0	89	− 87
2	334	330	3	137	175	3	110	, 115	6 8 0	51	52	0 14 1	67	−95
−1	998	862	−1	81	55	−1	219	−218	1	76	86	2 14 2	107	96
−2	405	413	−2	65	−66	−2	84	−91	−1	52	43	4 14 −2	70	69
−3	253	−258	−4	117	−126	−3	129	−108	−2	110	108	0 15 1	62	−67
2 2 0	308	307	3 4 0	200	187	−4	132	−139	1 9 0	119	124	4 15 1	87	80
2	113	114	1	95	89	4 6 0	71	−75	1	60	63	2 15 −1	89	−89
−1	204	194	2	197	−196	1	156	−157	2	189	−168	1 16 0	67	−90
−2	65	40	−1	434	−427	−1	234	221	3	140	−94			
−3	129	−110	−2	73	83	−2	61	−58	−1	99	113			

aperture of the lamp of the polarising microscope by which it was viewed, or by warming with the fingers) eventually produced single crystals. Bond's [5] corrections for absorption were applied to this set, which consisted of 398 independent non-zero values, compared with 560

[5] Bond, *Acta Cryst.*, 1959, **12**, 381; "International Tables for *X*-ray Crystallography," Kynoch Press, Birmingham, 1959, Vol. II.

in set (*A*); the smaller number is due to the heavier background associated with molybdenum radiation. Weissenberg photographs about four axes were used for (*A*) and about three for (*B*). The four films (Ilford Industrial G) simultaneously exposed were interleaved with 0·001 in. copper foil when molybdenum radiation was used, to give an effective film factor of about 3.

The *R* factor between sets (*A*) and (*B*) of F_{obs} was 17·7%.

Solution of the Structure.—The structure was determined from Patterson projections with the help of trial-and-error methods, and refined initially by (F_o–F_c) syntheses on four projections and later by three-dimensional least-squares analysis on a Pegasus computer, the Leeds programme being used which refines atomic co-ordinates, anisotropic vibrations, and scale factor. Five cycles reduced the *R* factor from 40% to 17% (calculated on the non-zero F_{obs} only). The bond lengths of this structure (*A*) were scarcely credible: the P–N bonds, for example, ranged from 1·38—1·65 Å in an unsystematic way. This refinement used F_{obs} values derived from intensities (*A*), and the disappointing results were the reason for measuring the new set (*B*). The new F_{obs} were scaled layer-line by layer-line with the calculated values of structure (*A*) and, by using them, five cycles of refinement reduced the *R* factor to 10·2% and gave the satisfactory structure (*B*) described below.

This situation seems surprising. It is not unexpected that the values of U_{ij}, the components of the tensor which defines the anisotropic thermal vibrations, would be spurious when based on F_{hkl} whose errors are distributed anisotropically, but it was hoped that this error distribution would not have any very serious effect on the atomic co-ordinates, and also that if such an effect were in fact present it would be revealed by large values of the co-ordinate standard deviations σ. Both these hopes were disappointed. If the values of the co-ordinates in the satisfactory structure (*B*) are taken for this purpose as correct, so that the differences between (*A*) and (*B*) are considered as errors in (*A*), 6 out of the 24 independent co-ordinates in (*A*) have errors greater than 3·2 σ and the largest is 8·1 σ. If σ is a true measure of the standard deviation, these errors, which are associated with the light nitrogen and fluorine atoms, are most unlikely; hence in this case σ has been grossly underestimated. It is no criticism of Cruickshank's [6] method of calculating standard deviations to point out that if used with systematically unreliable data it gives unreliable results, but it seems worth emphasising that when systematic errors are present the calculated values of σ may be worthless.

Values of F_{obs} of set (*B*) and F_{calc} are listed in Table 1.

TABLE 2.

Co-ordinates of atoms (Å).

	Monoclinic axes			Orthogonal axes		
	x	*y*	*z*	*x'*	*y'*	*z'*
P(1)	1·4282	1·0489	1·6185	1·3462	1·0489	1·1418
(2)	1·3890	−1·5562	0·3949	1·3093	−1·5562	−0·0687
N(1)	0·0022	1·6822	0·8061	0·0021	1·6822	0·8054
(2)	1·8320	−0·3079	1·2794	1·7268	−0·3079	0·6679
F(1)	2·5673	−1·9050	−0·1983	2·4199	−1·9050	−1·0553
(2)	1·5083	−2·7107	1·3840	1·4217	−2·7107	0·8805
(3)	1·6340	1·1411	3·2048	1·5402	1·1411	2·6594
(4)	2·5556	2·0103	1·5514	2·4089	2·0103	0·6983

TABLE 3.

Standard deviations of co-ordinates (Å).

	Monoclinic axes			Orthogonal axes			
	σ(*x*)	σ(*y*)	σ(*z*)	σ(*x'*)	σ(*y'*)	σ(*z'*)	σ(ζ)
P(1)	0·0044	0·0043	0·0052	0·0041	0·0043	0·0054	0·0051
(2)	0·0049	0·0046	0·0063	0·0046	0·0046	0·0065	0·0060
N(1)	0·0149	0·0166	0·0229	0·0140	0·0166	0·0234	0·0212
(2)	0·0186	0·0147	0·0192	0·0175	0·0147	0·0202	0·0191
F(1)	0·0124	0·0151	0·0151	0·0117	0·0151	0·0156	0·0149
(2)	0·0188	0·0122	0·0163	0·0177	0·0122	0·0175	0·0168
(3)	0·0163	0·0138	0·0146	0·0154	0·0138	0·0156	0·0153
(4)	0·0116	0·0118	0·0149	0·0109	0·0118	0·0154	0·0143

[6] Cruickshank, *Acta Cryst.*, 1949, **2**, 65.

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The Structure

The co-ordinates of the atoms are given in Table 2, where x, y, z are referred to the monoclinic crystal axes, and x', y', z' to orthogonal axes given by the transformation $x' = x \sin \beta$, $y' = y$, $z' = z + x \cos \beta$. Table 3 shows the estimated standard deviations of the atoms with respect to both co-ordinate systems. Table 4 shows the components of the vibration tensor U_{ij} with respect to x, y, z, for each atom, and Table 5 their standard deviations. Bond lengths and angles are given in Tables 6 and 7 with their estimated standard deviations σ. $\sigma(\phi)$ was calculated from the equation (due to D. F. Carroll):

$$\begin{aligned}(r_1 r_2 \sin\phi)^2\sigma^2(\phi) = {} & [(x_3 - x_2) - (x_1 - x_2)r_2 \cos\phi/r_1]^2\sigma^2(x_1) \\ & + [(x_1 - 2x_2 + x_3) - (x_1 - x_2)r_2 \cos\phi/r_1 - (x_3 - x_2)r_1 \cos\phi/r_2]^2\sigma^2(x_2) \\ & + [(x_1 - x_2) - (x_3 - x_2)r_1 \cos\phi/r_2]^2\sigma^2(x_3) \\ & + \text{corresponding terms in } y \text{ and } z.\end{aligned}$$

Table 4.

Components U_{ij} of vibration tensors (Å²).

	U_{11}	U_{22}	U_{33}	U_{13}	U_{23}	U_{12}
P(1)	0·0544	0·0565	0·0667	−0·0181	−0·0256	0·0284
(2)	0·0650	0·0509	0·0906	0·0292	0·0116	0·0425
N(1)	0·0728	0·0703	0·1283	0·0025	−0·0846	−0·0294
(2)	0·1016	0·0553	0·0767	0·0120	−0·0164	−0·0044
F(1)	0·0872	0·1413	0·1383	0·0797	−0·0282	0·0916
(2)	0·1988	0·0615	0·1235	0·0300	0·0540	0·0511
(3)	0·1314	0·1284	0·0790	−0·0459	−0·0728	0·0739
(4)	0·0931	0·0837	0·1218	−0·0542	−0·0171	0·1022

Table 5.

Standard deviations in U_{ij}.

	$\sigma(U_{11})$	$\sigma(U_{22})$	$\sigma(U_{33})$	$\sigma(U_{13})$	$\sigma(U_{23})$	$\sigma(U_{12})$
P(1)	0·0024	0·0026	0·0030	0·0038	0·0049	0·0039
(2)	0·0028	0·0023	0·0038	0·0041	0·0055	0·0049
N(1)	0·0100	0·0103	0·0173	0·0153	0·0227	0·0211
(2)	0·0112	0·0089	0·0113	0·0164	0·0183	0·0156
F(1)	0·0084	0·0121	0·0136	0·0161	0·0186	0·0166
(2)	0·0144	0·0077	0·0123	0·0166	0·0151	0·0213
(3)	0·0107	0·0113	0·0090	0·0167	0·0169	0·0153
(4)	0·0082	0·0081	0·0108	0·0120	0·0144	0·0140

Table 6.

Bond lengths (Å).

	r	$\sigma(r)$		r	$\sigma(r)$
P(1)–N(1)	1·523	0·016	P(1)–F(3)	1·533	0·016
P(1)–N(2)	1·487	0·016	P(1)–F(4)	1·500	0·013
P(2)–N(1)′	1·510	0·017	P(2)–F(1)	1·526	0·015
P(2)–N(2)	1·508	0·017	P(2)–F(2)	1·499	0·016

Table 7.

Bond angles.

	ϕ	$\sigma(\phi)$		ϕ	$\sigma(\phi)$
N(1) $\widehat{\text{P}}$(1) N(2)	122·3	1·04	N(1) $\widehat{\text{P}}$(1) F(3)	107·8	0·99
N(1)′ $\widehat{\text{P}}$(2) N(2)	123·2	0·96	N(1) $\widehat{\text{P}}$(1) F(4)	107·1	0·83
			N(2) $\widehat{\text{P}}$(1) F(3)	109·8	0·98
P(1) $\widehat{\text{N}}$(1) P(2)′	147·1	1·36	N(2) $\widehat{\text{P}}$(1) F(4)	108·0	0·83
P(1) $\widehat{\text{N}}$(2) P(2)	147·2	1·43	N(2) $\widehat{\text{P}}$(2) F(2)	107·9	1·00
			N(1)′ $\widehat{\text{P}}$(2) F(2)	108·0	1·00
F(3) $\widehat{\text{P}}$(1) F(4)	99·5	0·86	N(2) $\widehat{\text{P}}$(2) F(1)	107·7	0·92
F(1) $\widehat{\text{P}}$(2) F(2)	100·3	0·90	N(1)′ $\widehat{\text{P}}$(2) F(1)	107·3	1·03

ϕ is the angle at atom (2), r_1 and r_2 the distances (1)—(2) and (2)—(3) respectively. This is a more exact form of Ahmed and Cruickshank's [7] expression.

There are no significant differences in bond lengths and angles of a given type, and the mean values are P–N = 1·507 ± 0·017 Å, P–F = 1·514 ± 0·015 Å, $\widehat{NPN}$ = 122·7° ± 1·0°, $\widehat{PNP}$ = 147·2° ± 1·4°, $\widehat{FPF}$ = 99·9° ± 0·9° and $\widehat{NPF}$ = 108·0° ± 1·0°. The striking features are the short length P–N and the large angle PNP. The sum of the two independent angles is 269·9° and this close approximation to 270° suggests that the ring may be planar. The deviations ζ of the nitrogen atoms from the plane of the phosphorus atoms are not significant and the standard deviations $\sigma(\zeta)$ of all the ring atoms in a direction normal to this plane were used to obtain weighting factors $1/\sigma^2(\zeta)$ for a least-squares calculation of the mean plane of the ring, the equation of which is

$$0{\cdot}4069x' + 0{\cdot}3811y' - 0{\cdot}8302z' = 0. \quad (1)$$

The pairs of fluorine atoms are distributed not quite symmetrically about the plane, and this was still true even when the mid-points of F(1)–F(2) and F(3)–F(4) were included in another weighted least-squares calculation. It was concluded that the plane of the ring

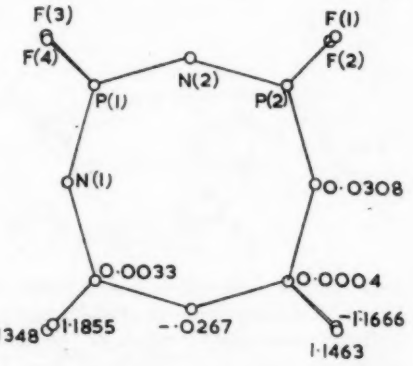

FIG. 1. Projection of the molecule in a direction perpendicular to the mean plane of the ring. Distances in Å from the plane are shown.

was not quite a mirror for the fluorine atoms and that the best plane was therefore plane (1). Fig. 1 shows the projection of a molecule down the normal to this plane. The distances ζ of the atoms from the plane are shown in Fig. 1 and the standard deviations of these distances appear as $\sigma(\zeta)$ in Table 3. The molecule obviously has symmetry close to $4/mmm$ (D_{4h}). Exact symmetry would impose conditions on the molecular geometry in addition to the planarity of the ring and the equality of chemically similar bonds and angles already noted. These conditions are examined in turn and the experimental values of the parameters, with their standard deviations in parentheses, are listed in brackets. The last column gives the ratio of the discrepancy to its standard deviation, calculated before the figures had been rounded off. F(1) · · · · F(2)^r is the distance between F(1) and the reflection of F(2) in the plane of the ring; cf. 0 is the origin at the centre of the molecule.

(*a*)	P(1) · · · 0 = P(2) · · · O	[2·053 (0·005); 2·035 (0·005)]	2·83
(*b*)	N(1) · · · 0 = N(2) · · · O	[1·865 (0·018); 1·877 (0·021)]	0·42
(*c*)	P(1) $\widehat{0}$ P(2) = 90°	[89·28° (0·19)]	3·79
(*d*)	N(1) $\widehat{0}$ N(2) = 90°	[89·61° (0·68)]	0·57
(*e*)	P(1) $\widehat{0}$ N(1) = 45°	[45·45° (0·48)]	0·94
(*f*)	F(1) · · · F(2)^r = 0	[0·108 (0·021)]	5·16
(*g*)	F(3) · · · F(4)^r = 0	[0·086 (0·019)]	4·48

The significant discrepancies are in (*a*), (*c*), (*f*), and (*g*), notably the last two.

The intermolecular contacts are:

Contact	$F(1)\cdots F(4)'$	$F(2)\cdots F(3)'''$	$F(2)\cdots F(4)'''$	$F(1)\cdots F(3)'$
Distance (Å)	3·01	3·13	3·23	3·29
Contact	$N(2)\cdots F(3)'''$	$N(2)\cdots F(4)'$	$N(1)\cdots F(4)''$	
Distance (Å)	3·49	3·57	3·58	

All other intermolecular F · · · F distances are greater than 3·4 Å. The values listed are all very large compared with those predicted from Pauling's values of van der Waals radii (2·70 Å for F · · · F and 2·85 Å for N · · · F). This suggests that the fluorine atoms may be charged. The three shortest separations are shown by broken lines (two curved to prevent confusion) in Fig. 2, which is the projection of the structure down the *b* axis. The non-zero values of $F\cdots F'$ can be explained qualitatively if it is assumed that F(1) and F(4)′, the atoms of the shortest contact, experience a mutual repulsion. From Fig. 1 it is seen that the major distortions (*f*) and (*g*) can be described approximately as (*f*) a small rotation about P(2) of the triangle P(2) F(1) F(2) in its plane in the direction F(1) ⟶ F(2) and (*g*) a small rotation of the triangle P(1) F(3) F(4) about an axis through P(1) and in its plane, thereby twisting its plane and bringing F(4) closer to N(1). With

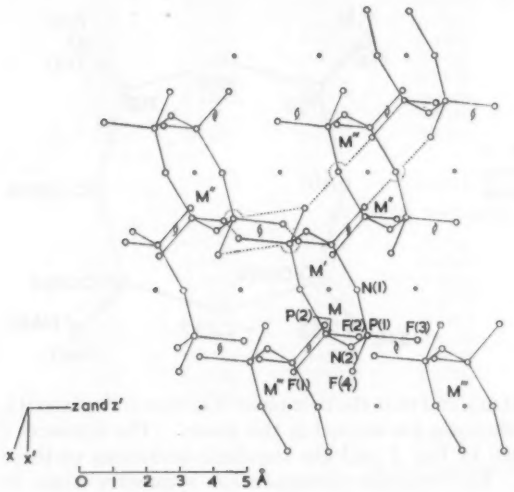

FIG. 2. The structure projected down the b axis. The three shortest intermolecular contacts are shown by broken lines.

the help of models it can be seen that these effects would be predictable from a postulated mutual repulsion of F(1) and F(4), if the triangles are considered rigid and anchored at the phosphorus atom. The reason for the differences in the two cases is that $F(1)\cdots F(4)'$ makes only a small angle with the plane through P(2), F(1), and F(2), but a much larger one with that through P(1), F(3), and F(4). It is suggested that this distortion might push the phosphorus atoms out of their natural positions and that this might account for the small but significant discrepancies in the values of $P(1)\cdots 0$, $P(2)\cdots 0$, and $P(1)\widehat{0}P(2)$.

If this is accepted, the molecule in its free state can be considered to have full $4/mmm$ symmetry and could be represented by Fig. 3.

The mean P–F bond length (1·51 Å) agrees well with the mean values in the phosphorus oxyhalides studied by Brockway and Beach.[9]

The P–N bond lengths are equal and short (1·51 Å). The purest P–N single bond

[7] Ahmed and Cruickshank, *Acta Cryst.*, 1953, **6**, 385.
[8] Pauling, " The Nature of the Chemical Bond," 2nd edn., Oxford, 1950.
[9] Brockway and Beach, *J. Amer. Chem. Soc.*, 1938, **60**, 1836.

reported is that in $NaHPO_3(NH_2)$ (1·78 Å) although this is a zwitterion structure;[10] Nordman's value[11] (1·635 Å) in $(H_2N)_3PBH_3$ will be modified by the charge which the phosphorus atom carries, at least formally. A more proper comparison is with the analogous values obtained by Wilson and Carroll[12] (1·59 Å) in $(PNCl_2)_3$ and Ketelaar and de Vries[2] (1·67 Å) in $(PNCl_2)_4$. The completely planar ring, which is quite unexpected, is made possibly by the unusually large angle (147°) at the nitrogen atoms, which therefore appear to be partially deficient in their lone-pair electrons.

The effect on the PN skeleton of substituting fluorine for chlorine is shown in the following Table.

Compound	Ring	P–N	$\widehat{PNP}$	$\widehat{NPN}$	$\widehat{RPR}$
$(PNCl_2)_4$	puckered	1·67 Å	123°	117°	105·5°
$(PNF_2)_4$	planar	1·51	147·2°	122·7°	99·9°

Another crystalline form is obtained at low temperature with the same space group $P2_1/a$ and the same unit-cell dimensions except that c is doubled. The reflections appearing on the extra layer-lines are very weak and the reflections common to both forms have very similar intensities. In the low-temperature form molecular symmetry $\bar{1}$ is no longer

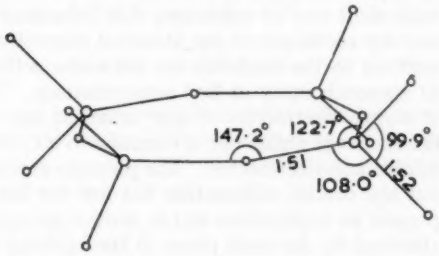

FIG. 3. The idealised molecule with mean values of bond lengths and angles.

mplied, but the crystal structure is obviously very similar to that described above. One explanation is that the molecules in the high-temperature form are distorted in a " chair-like " way while those in the low-temperature form have " boat-like " distortions; another is that the high-temperature form is composed of molecules with " boat-like " distortion distributed in a statistically disordered way. If the boat form has in itself 2 or m symmetry, which would seem likely, a superposition of two molecules to give a mean structure with a planar ring would not give mean positions of fluorine atoms asymmetrically disposed on either side of the ring and thus the hypothesis of disorder seems less likely, on admittedly speculative grounds. In any case the distortions must be small and would be unlikely to affect the conclusion that in its free state the molecule would have $4/mmm$ symmetry.

We are grateful to J. K. Leary for the optical data.

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[11] Nordman, *Acta Cryst.*, 1960, **13**, 535.
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943. *Absorption of Electrolytes by Ion-exchange Materials.*

By F. L. Tye.

A modified thermodynamic treatment of electrolyte absorption by an ion-exchange resin is presented which takes account of the potential gradient existing in the resin. As a result, the decrease of the mean activity coefficient of the absorbed electrolyte to low values in dilute solution is explained. An equation, which relates the concentrations of absorbed and external electrolyte, is deduced and shown to agree with experimental results over a wide range of crosslinking and concentration by appropriate choice of a single parameter.

A number of studies [1-5] have been made on the concentration of electrolyte absorbed by an ion-exchange resin in contact with an electrolyte. The remarkable feature of all these investigations is that in dilute solution the concentration of electrolyte absorbed in the resin phase is much greater than would be expected from simple electrolyte theory. An equivalent way of expressing this behaviour is to state that in dilute solutions the mean activity coefficient of the absorbed electrolyte tends to very low values. This is in sharp contrast to the tendency for the mean activity coefficient of simple electrolyte solutions to approach unity at low concentrations. The decrease of the mean activity coefficient of simple electrolytes to low values at low electrolyte concentrations is not confined to ion-exchange resins but is common to all systems in which fixed charges are present, *e.g.*, soluble polyelectrolytes. The phenomenon is obviously connected with the fixed charges, but the precise explanation has not yet been given. It is the purpose of this paper to present an explanation and to deduce an equation relating the concentration of electrolyte absorbed by the resin phase to the external concentration.

Freeman [6] attempted to prove that the phenomenon of low mean activity coefficients at low concentrations is unreal and merely due to incomplete separation of the ion-exchange resin from the external electrolyte in the experimental technique. The original workers [1,5] rejected this possibility. One difficulty in Freeman's approach is that the amount of external solution not separated from the resin is not constant for one experimental technique. Thus, using Davies and Yeoman's results [5] on a 5·5% divinylbenzene resin, Freeman [6] has to assume that the ratio of external to internal water for the separated resin is 0·036 for hydrochloric acid but 0·087 for potassium chloride. If Freeman's procedure is applied to lightly crosslinked resins the position becomes absurd. For ammonium chloride and a 2% divinylbenzene resin,[1] for example, it is necessary to assume a ratio of external to internal water of 0·6 to avoid low mean activity coefficients at low concentrations. For ammonium chloride and a 0·4% divinylbenzene resin [3] an even larger amount of external water has to be assumed. Further evidence of the reality of the low mean activity coefficients can be obtained from the work of Mackie and Meares [7] who used a single piece of ion-exchange material and so diminished the possibility of separation errors. Finally, as already mentioned, low mean activity coefficients are obtained with soluble polyelectrolytes and in this case phase separations are not involved.

Symbols.—*A* Concentration of fixed charges (g. equiv./l.), appropriate to the external concentration.

[1] Gregor, Gutoff, and Bregman, *J. Colloid Sci.*, 1951, **6**, 245.
[2] Gregor and Gottlieb, *J. Amer. Chem. Soc.*, 1953, **75**, 3539.
[3] Gottlieb, Ph.D. Thesis, Polytechnic Institute of Brooklyn, 1953.
[4] Pepper, Reichenberg, and Hale, *J.*, 1952, 3129.
[5] Davies and Yeoman, *Trans. Faraday Soc.*, 1953, **49**, 968.
[6] Freeman, *J. Phys. Chem.*, 1960, **64**, 1048.
[7] Mackie and Meares, *Proc. Roy. Soc.*, 1955, *A*, **232**, 485.

a Activity. c Concentration (g. equiv./l.).
e Electron charge. f Activity coefficient.
k Boltzmann's constant. P Pressure. R Gas constant.
T Absolute temperature. V Partial molar volume. z Valency.
β Fraction of pore space at zero electrical potential. F The Faraday
μ° Chemical potential in standard state.
ν Moles of ion from 1 mole of electrolyte.
ψ Electrical potential.

Unbarred symbols refer to the external electrolyte and barred ones to the resin phase. Subscripts c and o refer to counter- and co-ions, respectively, + and − to positive and negative ions respectively, and ± to mean values. Where c or $\bar{c}$ appears with no subscript it refers to concentration of external or absorbed electrolyte, respectively.

Classical Theory.—In the classical thermodynamic treatment the electrochemical potentials of the cations and of the anions in an ion-exchange material and external electrolyte are respectively set equal at equilibrium. Thus,

$$\mu^\circ_+ + \boldsymbol{R}T \ln a_+ + z_+\psi\boldsymbol{F} + PV_+ = \bar{\mu}^\circ_+ + \boldsymbol{R}T \ln \bar{a}_+ + z_+\bar{\psi}\boldsymbol{F} + \overline{P}\overline{V}_+ \quad (1)$$

and

$$\mu^\circ_- + \boldsymbol{R}T \ln a_- + z_-\psi\boldsymbol{F} + PV_- = \bar{\mu}^\circ_- + \boldsymbol{R}T \ln \bar{a}_- + z\bar{\psi}\boldsymbol{F} + \overline{P}\overline{V}_- \quad (2)$$

If $PV^+ - \overline{P}\overline{V}_+$ and $PV_- - \overline{P}\overline{V}_-$ are assumed to be negligible, as is permissible for small ions, the standard state of the resin phase is made the same as that of the external solution, namely infinite dilution, so that $\mu^\circ_+ = \bar{\mu}^\circ_+$, and $\mu^\circ_- = \bar{\mu}^\circ_-$; and if the electrical potential in the external phase is taken as zero; then equations (1) and (2) reduce to

$$\boldsymbol{R}T \ln a_+ = \boldsymbol{R}T \ln \bar{a}_+ + z_+\bar{\psi}\boldsymbol{F} \quad (3)$$

and

$$\boldsymbol{R}T \ln a_- = \boldsymbol{R}T \ln \bar{a}_- + z_-\bar{\psi}\boldsymbol{F}. \quad (4)$$

By combining equations (3) and (4) with the relation

$$\nu_+z_+ + \nu_-z_- = 0, \quad (5)$$

the usual Donnan expression is obtained

$$a_+^{\nu_+}a_-^{\nu_-} = \bar{a}_+^{\nu_+}\bar{a}_-^{\nu_-}. \quad (6)$$

Equation (6) may be rewritten

$$(A + \bar{c})^{\nu_c}\bar{c}^{\nu_o} = c^{\nu_c+\nu_o}(f_\pm/\bar{f}_\pm)^{\nu_c+\nu_o} \quad (7)$$

to give the relation used to calculate the mean activity coefficient in the resin phase from experimental results. This activity coefficient, $\bar{f}_\pm$, will be termed the Donnan mean activity coefficient to distinguish it from another which appears in the new treatment.

New Treatment.—To understand the reason for the unexpected behaviour of the Donnan mean activity coefficient, $\bar{f}_\pm$, consider equations (3) and (4) again. The final Donnan expression (6) is obtained from these, with the help of equation (5), by eliminating the electrical potential $\bar{\psi}$. This implies that $\bar{\psi}$ is constant throughout the resin phase. It is however firmly established [8,9] that, in the vicinity of fixed charges, electrical potential changes continuously, from a numerically high value adjacent to the charges to zero or a numerical minimum in more remote regions. A consequence of this is that, on average,

[8] Corkill and Rosenhead, *Proc. Roy. Soc.*, 1939, *A*, **172**, 410.
[9] Verwey and Overbeek, "Theory of the Stability of Lyophobic Colloids," Elsevier Publishing Company, New York, 1948.

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the cations in the resin phase are at a lower potential than the anions. Hence the $\bar{\psi}$ term in equations (3) and (4) must be replaced by two unequal terms $\bar{\psi}_+$ and $\bar{\psi}_-$.

Thus, $$\boldsymbol{RT} \ln a_+ = \boldsymbol{RT} \ln \bar{a}_+ + z_+\bar{\psi}_+\boldsymbol{F} \quad (8)$$

and $$\boldsymbol{RT} \ln a_- = \boldsymbol{RT} \ln \bar{a}_- + z_-\bar{\psi}_-\boldsymbol{F}. \quad (9)$$

The double bar is used in the resin phase to distinguish activities and activity coefficients arising in the present treatment from those which appear in the classical theory.

Combining equations (5), (8), and (9) we have

$$\ln a_+^{\nu_+} a_-^{\nu_-} = \ln \bar{a}_+^{\nu_+} \bar{a}_-^{\nu_-} + \boldsymbol{F}(z_+\nu_+\bar{\psi}_+ + z_-\nu_-\bar{\psi}_-)/\boldsymbol{RT}. \quad (10)$$

Now, by substitution from equation (6) and rearrangement

$$\bar{f}_\pm = f_\pm \exp\left[\frac{\boldsymbol{F}(z_+\nu_+\bar{\psi}_+ + z_-\nu_-\bar{\psi}_-)}{\boldsymbol{RT}(\nu_+ + \nu_-)}\right]. \quad (11)$$

It is now apparent that the Donnan mean activity coefficient, $\bar{f}_\pm$, contains a potential term, and it is this term which is responsible for the low values in dilute solutions. The other activity coefficient, $\bar{\bar{f}}_\pm$ is independent of potential terms arising from the presence of fixed charges and is therefore more akin to the activity coefficients of simple electrolyte solutions. It is convenient to call, $\bar{\bar{f}}_\pm$ the Debye–Hückel mean activity coefficient. Let us now consider the potential term. At high concentrations the fixed charges are screened and as a result the differences of potential within the resin are small. Thus $\bar{\psi}_+$ and $\bar{\psi}_-$ tend to equality, the exponential power term tends to zero and the value of $\bar{f}_\pm$ approaches that of $\bar{\bar{f}}_\pm$.

At low concentrations the fixed charges cause potential gradients in the pores of the ion-exchange resin. As a result, the centre of gravity of the cations is at a lower potential than the centre of gravity of the anions; the exponential power term in equation (11) is therefore negative and the exponential itself less than unity so that $\bar{f}_\pm$ is less than $\bar{\bar{f}}_\pm$. Thus, although the Debye–Hückel mean activity coefficient, $\bar{\bar{f}}_\pm$, may behave similarly to the activity coefficients of simple electrolyte solutions, the Donnan mean activity coefficient, $\bar{f}_\pm$, has a lower value, and, as the difference between $\bar{f}_\pm$ and $\bar{\bar{f}}_\pm$ increases as the concentration decreases, low values of the Donnan mean activity coefficient are to be expected in dilute solutions.

An Equation relating Internal and External Electrolyte Concentration.—It is apparent from the foregoing that any successful theoretical treatment of the concentration of absorbed electrolyte must take into account the varying electrical potential in the resin phase. One approach to the problem is to assume a model for the ion-exchange material, determine the electrical potential distribution by solving the Poisson–Boltzmann equation,[10] then to use the Boltzmann distribution law to calculate ionic distribution and finally integrate this to obtain the average concentration of absorbed electrolyte. This has been done by Lazare, Sundheim, and Gregor,[11] and by Klaarenbeek,[12] who used infinite parallel charged plates as the model for the ion-exchange material. Unfortunately the final expressions are complicated and therefore difficult to use in practice. A much simpler treatment is presented here. The variation of electrical potential is taken into account by averaging it into two levels, one of which is zero. Other than this, no particular model is assumed for the ion-exchange material.

The pore space in the ion-exchange material is divided into a fraction $1 - \beta$ at an

[10] Booth, *J. Chem. Phys.*, 1951, **19**, 821.
[11] Lazare, Sundheim, and Gregor, *J. Phys. Chem.*, 1956, **60**, 641.
[12] Klaarenbeek, quoted by Overbeek in "Progress in Biophysics and Biophysical Chemistry" (Ed. Butler), Pergamon Press, London, 1956, Vol. 6, p. 57.

electrical potential $\bar{\psi}$ and a fraction β at zero electrical potential. The division of the pore space into the two regions is not considered to have physical reality and it is not suggested that there necessarily exists any portion of pore space at zero potential. The division is merely a mathematical device to introduce two potential levels which constitute a better representation than the single potential level of the classical treatment.

The concentrations of ions in each region are given by the Boltzmann distribution law. At potential $\bar{\psi}$, the concentration of cations is $c \exp(-z_+e\bar{\psi}/kT)$ and the concentration of anions is $c \exp(-z_-e\bar{\psi}/kT)$. In the pore space at zero potential the concentrations of cations and anions are, of course, both c. The two pore space fractions being taken together, the " average " concentrations of cations and anions are:

$$\bar{c}_+ = \beta c + (1 - \beta)c \exp(-z_+e\bar{\psi}/kT) \quad (12)$$

and

$$\bar{c}_- = \beta c + (1 - \beta)c \exp(-z_-e\bar{\psi}/kT). \quad (13)$$

Eliminating $\bar{\psi}$ from equations (12) and (13), we have

$$[(\bar{c}_+ - \beta c)/(1 - \beta)c]^{z_-} = [(c_- - \beta c)/(1 - \beta)c]^{z_+} \quad (14)$$

or

$$[(c_0 - \beta c)/(1 - \beta)c]^{z_0} = [(c_0 - \beta c)/(1 - \beta)c]^{z_0}. \quad (15)$$

Substituting $A + \bar{c} = \bar{c}_0$ in equation (15) and rearranging gives

$$[\bar{c} - \beta c]^{1-z_0/z_0} + A[\bar{c} - \beta c]^{-z_0/z_0} - [(1 - \beta)c]^{1-z_0/z_0} = 0. \quad (16)$$

This is the general equation.

When $z_0 + z_0 = 0$, equation (16) reduces to a quadratic in $(\bar{c} - \beta c)$:

$$(\bar{c} - \beta c)^2 + A(\bar{c} - \beta c) - (1 - \beta)^2c^2 = 0, \quad (17)$$

the positive root of which is

$$\bar{c} = \beta c - A/2 + \sqrt{[A^2/4 + (1 - \beta)^2c^2]}. \quad (18)$$

Equation (18) applies to 1 : 1 and 2 : 2 electrolytes and relates the concentration of absorbed electrolyte to the external concentration. It contains one unknown parameter, β. In this sense it is not inferior to the more complex approach of Lazare, Sundheim, and Gregor,[9] and Klaarenbeek,[10] which also yields an equation containing an unknown parameter, namely the separation of the infinitely charged plates used as the model for the ion-exchange material.

To test whether equation (18) is of the right type, an expression for $\bar{f}_\pm/f_\pm$ is obtained by substituting equation (18) in equation (7), remembering that $\nu_0 = \nu_0$.

Thus,

$$(\bar{f}_\pm/f_\pm)^2 = [1 + 2\beta\{\beta - 1 + \sqrt{[A^2/4c^2 + (1 - \beta)^2]}\}]^{-1}. \quad (19)$$

When $c \longrightarrow 0$, $A/2c \longrightarrow \infty$, and $\bar{f}_\pm/f_\pm \longrightarrow 0$; the requirement of $\bar{f}_\pm$ tending to low values at low concentration is therefore satisfied. When c is large, $(A/2c)^2 \ll (1 - \beta)^2$, and $\bar{f}_\pm/f_\pm \longrightarrow 1$; this also is in agreement with experiment.[2] One further comparison with experiment supports the general satisfactory nature of equation (18). As c tends to zero, equation (18) indicates that $\bar{c}/c$ tends to the constant value of β. The recent results of Freeman [6] show clearly that experimentally $\bar{c}/c$ does indeed tend to a constant value as c decreases.

Detailed Comparison with Experiment.—For detailed comparison of equation (18) with experiment, the studies on the absorptions of hydrogen and alkali-metal chlorides by polystyrenesulphonate resins, crosslinked with various percentages of divinylbenzene, have been chosen, as these are the most comprehensive available.

The comparisons are shown in Figs. 1—4. The experimental results are in molalities and the terms c and $\bar{c}$ in equation (18) have been considered to be in these units also. The agreement with ammonium chloride is very good at all divinylbenzene contents. For the

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sake of clarity, comparisons for 0·4 and 17% divinylbenzene have been omitted from Fig. 1, although the agreement with these is equally good. There is reasonable agreement with potassium chloride. For lithium chloride the coincidence is good with 2% divinylbenzene

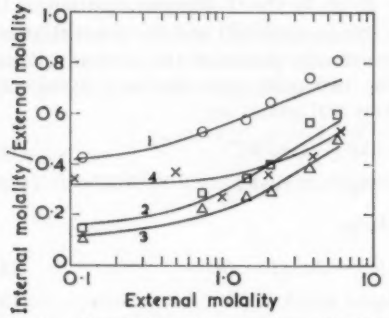

FIG. 1. Absorption of ammonium chloride.

2% DVB: ○ experimental, ref. 1; curve 1, calculated $\beta = 0{\cdot}40$. 6% DVB: □ experimental, ref. 1; curve 2, calculated $\beta = 0{\cdot}15$. 10% DVB: △ experimental, ref. 1; curve 3, calculated $\beta = 0{\cdot}12$. 26% DVB: × experimental, ref. 3; curve 4, calculated $\beta = 0{\cdot}31$.

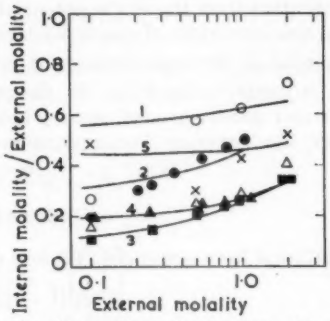

FIG. 2. Absorption of potassium chloride.

2% DVB: ○ experimental, ref. 2; curve 1, calculated $\beta = 0{\cdot}55$. 2·25% DVB: ● experimental, ref. 5; curve 2, calculated $\beta = 0{\cdot}29$. 5·5% DVB: ■ experimental, ref. 5; curve 3, calculated $\beta = 0{\cdot}12$. 10% DVB: △ experimental, ref. 2; ▼ experimental, ref. 5; curve 4, calculated $\beta = 0{\cdot}19$. 26% DVB: × experimental, ref. 2; curve 5, calculated $\beta = 0{\cdot}45$.

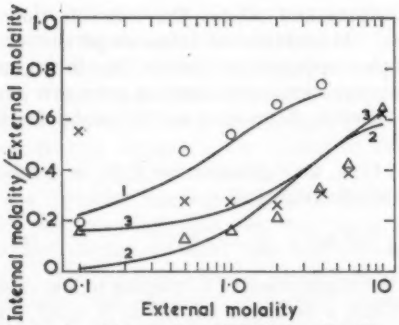

FIG. 3. Absorption of lithium chloride.

2% DVB: ○ experimental, ref. 3; curve 1, calculated $\beta = 0{\cdot}17$. 10% DVB: △ experimental, ref. 3; curve 2, calculated $\beta = 0$. 26% DVB: × experimental, ref. 3; curve 3, calculated $\beta = 0{\cdot}15$.

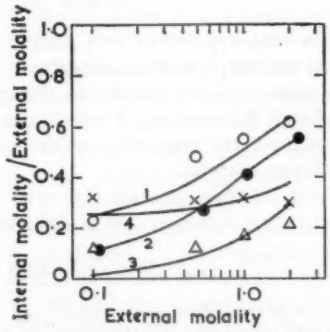

FIG. 4. Absorption of hydrochloric acid.

2% DVB: ○ experimental, ref. 2; curve 1, calculated $\beta = 0{\cdot}20$. 2% DVB: ● experimental, ref. 4; curve 2, calculated $\beta = 0{\cdot}06$. 10% DVB: △ experimental, ref. 2; curve 3, calculated $\beta = 0$. 26% DVB: × experimental, ref. 2; curve 4, calculated $\beta = 0{\cdot}25$.

resin but is not so satisfactory at the higher crosslinkages. With hydrochloric acid the agreement is again good at all crosslinkages when the results of Gregor *et al.*[2] are used. However, no choice of β is possible that will give any sort of agreement with the results of Pepper, Hale, and Reichenberg[4] on 5% and 10% divinylbenzene resins or with those of Davies and Yeoman[5] on a 5·5% divinylbenzene resin supplied by Pepper. The results of Pepper *et*

al.[4] do, however, agree with equation (18) for a 2% divinylbenzene resin. The disagreement between Gregor *et al.* and Pepper *et al.* for hydrochloric acid at all cross-linkages and between the former workers [3] and Davies and Yeoman [5] for potassium chloride at 2—2·5% crosslinking is far outside experimental error and further clarification is necessary. The results of Gregor *et al.*[1-3] with 26% divinylbenzene resins are also surprising in that they all show electrolyte absorptions greater than those obtained with some of the resins of lower crosslinking.

Gregor and his co-workers [1-3] also give some figures for absorption from external solutions less than 0·1M which suggest that equation (18) fails at external concentrations below 0·1M. Many of the experimental results in this region are difficult to understand, however, and it is possible that the data, and not the equation are at fault. Thus, the steady downward trend of $\bar{c}/c$ as the external concentration is decreased is suddenly reversed below 0·1M, and in some cases the value of $\bar{c}/c$ in the region of 0·01M is three or four times as great as that at about 0·1M. In one instance, that of 0·01M-lithium chloride

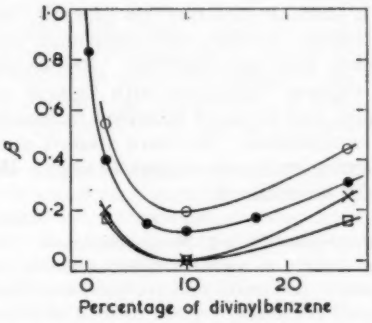

FIG. 5. β Values.
● NH_4Cl. ○ KCl. □ LiCl. × HCl.

n equilibrium with a 26% divinylbenzene resin,[3] the concentration of absorbed electrolyte is actually given as greater than the external concentration. Freeman [6] has suggested that this effect is due to absorption by impurities in the resin.

In spite of the minor disagreements noted, and the extreme simplicity of the theoretical treatment being considered, equation (18) gives good agreement at all divinylbenzene contents and over a wide range of concentration. It is, perhaps, surprising that the use of a constant value of β at all concentrations should be satisfactory. To some extent this is due to the form of equation (18) which is such that at high concentrations the value calculated for $\bar{c}$ is not very sensitive to the value assigned to β. The value of β can therefore be chosen to match the experimental results at the lower concentrations.

In Fig. 5 the values of β which give the best agreement with the results of Gregor and his co-workers [1-3] are plotted against the percentage of divinylbenzene in the resin. The values for ammonium chloride, which are the most extensive, fall on a smooth curve. It is satisfying that extrapolation of this curve indicates that at zero crosslinking β is unity. The β values for the other electrolytes fall on curves of similar shape. The decrease of β in the range of crosslinking 0—10% is understandable. As crosslinking increases, the concentration of fixed charges increases so that the potential in the resin is higher and hence the fraction β of pore space which is considered mathematically as being at zero potential, must decrease. The rise of β above 10% crosslinking is due to the surprising fact, already mentioned, that higher electrolyte absorptions were found experimentally for the 26% divinylbenzene resin than for the 10% divinylbenzene material.

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944. *Complex-forming Agents Similar to 2,2′-Bipyridyl. Part I. Some Ligands containing Imidazole.*

By F. Holmes, K. M. Jones, and E. G. Torrible.

A general study has been made of chelated complexes formed by 4-2′-pyridylimidazole and 2,2′-bi-imidazolyl. With neither ligand can stability constants of the metal complexes be evaluated conveniently by potentiometric titration. Two series of solid complexes are formed by each ligand, those from acid solution being in general similar to the corresponding compounds of bipyridyl, whereas those from alkaline solution are "inner complexes" formed by loss of the imidazole imino-hydrogen. The ferrous complex of bi-imidazolyl is yellow, not red.

2,2′-Bipyridyl is well known as an analytical reagent for ferrous iron and for a number of other metal ions in a lower valency state. Much less attention has been given to other bases of the type. Bailar and Busch,[1] and Stoufer and Busch,[2] studied compounds in which an imine structure was generally achieved by a $-C=NR$ side chain at the position 2 of pyridine. Studies with compounds containing heterocyclic rings other than pyridine, however, have been very few. Breckenridge[3] published the absorption spectra of ferrous and cuprous complexes with ligands containing quinoline, isoquinoline, or thiazole. Harkins and Freiser[4] described in greater detail the reactions of pyridyl-benzimidazole and -imidazoline. We have studied a number of other examples of the type, chiefly containing imidazole or thiazole rings. Here we describe work with 4-2′-pyridylimidazole and 2,2′-bi-imidazolyl.

Experimental

Materials.—(i) *4-2′-Pyridylimidazole.* 2-Acetylpyridine oxime was obtained by addition of the ketone to aqueous hydroxylamine hydrochloride, being liberated by addition of solid potassium carbonate and recrystallised from ether. From it the 4-2′-pyridylimidazole was prepared essentially by the method of Clemo *et al.*[5] The toluene-*p*-sulphonate of the oxime was treated with potassium in dry ethanol. We found it essential to keep the mixture cool at this stage or much of the 2-aminoacetylpyridine was lost.

The ligand itself was obtained from the final reaction as a yellowish gum. Recrystallisation of this from ether–light petroleum (seeding) gave crystals, m. p. 111·5° (Found: C, 66·4; H, 4·9; N, 29·0. Calc. for $C_8H_7N_3$: C, 66·2; H, 4·8; N, 29·0%).

(ii) *2,2′-Bi-imidazolyl.* Debus[6] prepared this compound by condensing ammonia and glyoxal. We found the yield to be greatly increased by preparing the glyoxal *in situ* from concentrated ammonia solution and the sodium salt of glyoxal bisulphite. The precipitated compound was recrystallised from a large volume of water (Found: C, 53·8; H, 4·6; N, 41·6. Calc. for $C_6H_6N_4$: C, 53·7; H, 4·5; N, 41·8%).

(iii) "AnalaR" dioxan was purified as described by Weissberger and Proskauer.[7] Other reagents, where possible, were of "AnalaR" grade, or they were purified by appropriate methods.

Determinations.—Dissociation constants for the ligands were obtained by potentiometric titration at 25·0° ± 0·1°. 5·00 ml. of *ca.* 0·1N-perchloric acid, 10·00 ml. of 10^{-2}M-aqueous solution of the organic base, and 35·00 ml. of air-free water were titrated with carbonate-free 0·1000N-sodium hydroxide. Stirring was by means of nitrogen, purified and saturated with aqueous vapour at 25·0°.

Attempts were made to obtain stability constants for the metal complexes from the results of similar titrations performed in the presence of metal ions added as their perchlorates, the metal : ligand molar ratio generally being 1 : 3.

Potentiometric Titrations: Determinations of Dissociation Constants.—pK's quoted are stoicheiometric and refer to ionic strength ~0·01M.

[1] Bailar and Busch, *J. Amer. Chem. Soc.*, 1956, **78**, 1137.
[2] Stoufer and Busch, *J. Amer. Chem. Soc.*, 1956, **78**, 6016.
[3] Breckenridge, *Canad. J. Chem.*, 1954, **32**, 512, 641.
[4] Harkins and Freiser, *J. Amer. Chem. Soc.*, 1956, **78**, 1143.
[5] Clemo, Holmes, and Leitch, *J.*, 1938, 953.
[6] Debus, *Annalen*, 1859, **107**, 199.
[7] Weissberger and Proskauer, "Organic Solvents," Oxford Univ. Press.

4-2′-Pyridylimidazole. The pK' of this compound under our conditions was 5·46. Up to a pH of 11·5 there was no evidence in the titration curve for dissociation of the imino-hydrogen atom. This is consistent with the known fact that it is difficult to remove this hydrogen and with the result obtained by Harkins and Freiser [4] in the titration of 2-2′-pyridyl-benzimidazole and -imidazoline. 4-2′-Pyridylimidazole is thus similar to 2,2′-bipyridyl, which is also monobasic under these conditions.

2,2′-Bi-imidazolyl. This compound and its complexes were very insoluble in cold water; the titrations were carried out in 50% (v/v) dioxan–water. The pH correction for this medium was made as given by Van Uitert and Haas [8] and by Holmes and Crimmin.[9] The pK' was 4·57. No other ionisation was found up to pH 11·5, so this compound also behaves as a mono-acidic base.

Potentiometric Titrations: Determination of Stability Constants.—With 4-2′-pyridylimidazole, complex formation began at quite low pH's, particularly with copper(II) and nickel(II), so that no great reliance could be placed on the results. When formation curves were plotted they were not symmetrical. For these reasons no stability constants were evaluated.

With 2,2′-bi-imidazolyl, chelation occurred at higher pH's but the formation curves were not completely symmetrical so that no stability constants are given.

The titration curves show that, in both cases, after neutralisation of all the acid present either as free acid or protonated base, continued titration is accompanied by further liberation of hydrogen ions. This could be due either to hydrolysis or to dissociation of the imino-hydrogen of the imidazole. It may well be due to the latter, as will be seen. It is not found when the ligand is titrated alone. It must be partly responsible for the dissymmetry in the upper part of the formation curves.

A more detailed study of the stability constants will be published later.

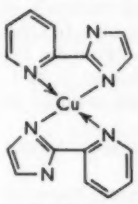
Solid Complexes of 4-2′-Pyridylimidazole.—Solid complexes were obtained by precipitation from an aqueous solution containing ligand and metal ion. They were identified by analysis and by conductance measurements. Metal analyses were by standard semimicro-gravimetric methods after destruction of the organic material by wet oxidation; water determinations were by loss of weight at 115° and, except for copper complexes, by Karl Fischer titration.

Copper complexes. Several compounds were obtained:

(1) Cupric ions and ligand in aqueous solution of pH <7 gave an intensely blue-green solution ($\lambda_{max.}$ 710 mμ), the coloured material not being extractable into pentyl alcohol. Addition of sodium chloride gave a bright green crystalline precipitate, insoluble in pentyl alcohol but soluble in hot water. The green *product* obtained after centrifugation, washing with cold water, and drying in a vacuum-desiccator and then at 115° was formulated as CuA_2Cl_2, where A = pyridylimidazole (Found: Cu, 15·0; C, 45·3; H, 2·8; N, 19·0; Cl, 16·9. $CuC_{16}H_{14}N_6Cl_2$ requires Cu, 15·0; C, 45·2; H, 3·3; N, 19·8; Cl, 16·7%). When dried *in vacuo*, it retained one molecule of water, which was removed on heating.

(2) A blue solid similarly obtained on addition of sodium perchlorate was the corresponding *perchlorate* [Found: Cu, 11·2; C, 35·3; H, 3·6; N, 15·8; ClO_4, 35·9. $CuC_{16}H_{14}N_6(ClO_4)_2$ requires Cu, 11·5; C, 34·8; H, 2·6; N, 15·2; ClO_4, 36·0%].

(3) When the aqueous suspension in (1) or (2) is warmed to dissolve the precipitate, and aqueous sodium hydroxide is added to pH 8—9, a blue, rather gelatinous precipitate is obtained. Centrifugation and washing with hot water (to remove cationic complex) gave a blue-green solid, insoluble in water but soluble in ethanol or pentyl alcohol (Found, in material dried at 105°: Cu, 17·8; C, 53·4; H, 3·7; N, 23·7; Cl or ClO_4, 0%). The analysis approximates to that required for CuR_2, where R represents pyridylimidazole less one hydrogen atom (Calc. for $CuC_{16}H_{12}N_6Cu$: Cu, 18·1; C, 54·6; H, 3·4; N, 23·9%).


(I)

The complexes from acid solution are those expected, being similar to those of bipyridyl; that obtained from slightly alkaline solution may be represented as an " inner complex " (I).

Such formulæ are supported by conductance measurements. (*a*) The diperchlorate and the corresponding complex obtained from bipyridyl had almost identical values of Λ_∞ in nitrobenzene, and plots of conductance against the square root of concentration had similar slopes. Both ligands gave values acceptable for a uni-bivalent electrolyte. (*b*) Values of Λ_∞ obtained

[8] Van Uitert and Haas, *J. Amer. Chem. Soc.*, 1953, **75**, 451.
[9] Holmes and Crimmin, *J.*, 1955, 3467.

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with the dichloride were much lower, but so were those for (Cu $bipy_2$)Cl_2; and the slopes were similar. The chloride, unlike the more ionic perchlorate, may be partly co-ordinated when nitrobenzene is used as a solvent. (*c*) A solution of the inner complex in nitrobenzene had a conductance too low to be measured. Values of Λ_∞ in nitrobenzene were: [Cu $(pyim)_2$]$(ClO_4)_2$ 60·0, [Cu $(bipy)_2$]$(ClO_4)_2$ 60·0, [Cu $(pyim)_2$]Cl_2 9·7, [Cu $(bipy)_2$]Cl_2 8·5, Cu (pyim − H)$_2$ 0·0.

(4) 2,2′-Bipyridyl gives well-defined complexes with copper(I), so the previous preparations were repeated in the presence of reducing agents. If hydroxylamine hydrochloride was present at pH <7, the cationic complexes were once more obtained, as might be expected. If, however, it was added before the solution was made alkaline during the preparation of the inner complex, then a light green flocculent precipitate was formed, insoluble in ethanol and pentyl alcohol, and differing from the other compounds. Preliminary work showed it to be probably a hydroxy-complex; it is being further investigated.

Nickel. At pH 4 a pink *complex* was precipitated on addition of an excess of aqueous sodium iodide to a 1 : 3 molar ratio of nickel chloride and ligand. This became buff when dried *in vacuo*, and proved rather soluble in hot water (Found: Ni, 7·0; C, 35·0; H, 3·8; N, 15·1; I, 31·3; H_2O, 7·5. $NiC_{24}H_{21}N_9I_2,4H_2O$ requires Ni, 7·2; C, 35·2; H, 3·6; N, 15·4; I, 31·0; H_2O, 8·8%).

Addition of aqueous sodium hydroxide to pH 8, after warming to dissolve the original precipitate, gave a pale green-blue precipitate. This *product* was analysed after drying *in vacuo* and is formulated as $NiR_2,2H_2O$ (R as above) (Found: Ni, 15·5; C, 50·6; H, 4·4; N, 22·1; I, 0; H_2O, 7·7. $NiC_{16}H_{12}N_6,2H_2O$ requires Ni, 15·3; C, 50·7; H, 4·2; N, 21·9; H_2O, 9·4%).

Cobalt. When an excess of aqueous sodium iodide was added to a solution of cobalt(II) chloride (1 mol.) and ligand (3 mols.) under conditions which prevented oxidation, a brown precipitate appeared which, after drying *in vacuo*, gave analyses corresponding to $CoA_2I_2,4H_2O$ (Found: Co, 6·9; C, 33·9; H, 3·6; N, 15·8; I, 34·3; H_2O, 7·8. $CoC_{24}H_{21}N_9I_2,4H_2O$ requires Co, 7·2; C, 35·1; H, 3·6; N, 15·4; I, 30·9; H_2O, 7·8%). Precipitation in aerobic conditions gave a precipitate of similar composition.

When this complex was dissolved by heating the solution and sodium hydroxide was then added, no inner complex was precipitated but the colour of the solution changed from pale buff to orange. The solution, on concentration, gave an orange deposit which, after drying and analysis, proved to be the cobalt(III) inner *complex* (Found: Co, 11·2; C, 58·6; H, 3·6; N, 25·9; halide, 0; sodium, 0. $CoC_{24}H_{21}N_9$ requires Co, 12·0; C, 58·7; H, 3·7; N, 25·7%).

If sodium hydroxide was added to a 1 : 2 (molar) mixture of cobalt(II) chloride and ligand, then at pH ~8 the cobalt(II) inner *complex* was obtained as a brown precipitate (Found: Co, 16·3; C, 52·0; H, 3·5; N, 23·4; Cl, 0. $CoC_{16}H_{12}N_6,H_2O$ requires Co, 16·1; C, 52·6; H, 3·9; N, 23·0%). When an attempt was made to wash this with ethanol it blackened. The complex was therefore heated with ethanol; an orange solution and a black precipitate of a hydrated cobalt oxide resulted. On evaporation, the orange solution gave the orange cobalt(III) inner complex once more.

Ferrous iron. Cationic *complexes* were prepared, as above. All were red, *e.g.*, $FeA_3I_2,3H_2O$ (Found: Fe, 7·1; C, 35·4; H, 3·6; N, 16·3; I, 32·3; H_2O, 6·3. $FeC_{24}H_{21}N_9I_2,3H_2O$ requires Fe, 7·0; C, 36·1; H, 2·9; N, 15·8; I, 31·8; H_2O, 5·8%).

When a 1 : 3 or a 1 : 2 molar ratio was used and the mixture made alkaline, a scarlet precipitate was first obtained which became brown when dry. It contained one molecule of ligand to each iron atom. This was a hydrolysed product which is being further investigated.

Ferric iron. A *complex*, $FeA_3I_3,3H_2O$, was prepared as a brown precipitate (Found: Fe, 6·0; C, 31·8; H, 2·7; N, 14·0; I, 39·6; H_2O, 5·9. $FeC_{24}H_{21}N_9I_3,3H_2O$ requires Fe, 6·0; C, 31·1; H, 2·5; N, 13·6; I, 41·1; H_2O, 5·8%). Attempts to produce an inner complex resulted in precipitation of ferric hydroxide.

Molar conductances in nitrobenzene were negligible for all the inner complexes. Values for some of the others are given in Table 1.

Both of our iron complexes gave low values for Λ_∞ in nitrobenzene. In water, however, the figures were much nearer those expected and it must be assumed that some association had occurred in nitrobenzene.

Solid Complexes of 2,2′-Bi-imidazolyl.—Again two series of complexes were isolated but the methods were modified slightly because the ligand was very much less soluble in water, and the cationic complexes were rather less soluble in hot water.

Copper. Bi-imidazolyl (0·1—0·2 g.) was dissolved in 0·1M-hydrochloric acid (10 ml.), and

TABLE 1.

Values of Λ_∞ in nitrobenzene for some cationic complexes.

Complex	Λ_∞	Ref.	Complex	Λ_∞	Ref.
$Ni(bipy)_3(ClO_4)_2$	79·0	*a*	$Fe(py\text{-}im)_3I_2$	39·5	*a*
$Ni(bipy)_3Cl_2$	66·0	*a*	$Fe(py\text{-}im)_3I_3$	48·0	*a*
$Ni(py\text{-}im)_3I_2$	73·5	*a*	$Rh(bipy)_3(ClO_4)_3$	~120	*b*
$Co(bipy)_3(ClO_4)_2$	78·5	*a*	$Fe(bipy)_3I_3$	57·8	*c*
	~75	*b*	$Cu(phenan)_3(ClO_4)_2$	43·1	*d*
$Co(py\text{-}im)_3I_2$	65·0	*a*	$[Rh(bipy)_3Cl_2]ClO_4$	~32	*b*

(*a*) Present work, valid for 25·0°. (*b*) Estimated from the data of Martin and Waind (*J.*, 1958, 4284), valid for 25°. (*c*) Nyholm and Harris (*J.*, 1956, 4377), valid for $2{\cdot}5 \times 10^{-4}$M and 20°. (*d*) *Idem, ibid.*, valid for $5{\cdot}0 \times 10^{-4}$M and 25°.

cupric sulphate added so that the ligand : metal molar ratio was >2 : 1. Aqueous sodium hydroxide was added to pH 3·5, the solution becoming intensely green and a small amount of green crystals appearing. These were the cationic complex; they were redissolved by addition of water and warming. An excess of solid sodium chloride was added, giving a bright green crystalline *complex*; this was centrifuged off, recrystallised from dilute sodium chloride solution, and dried *in vacuo* (Found: Cu, 15·2; Cl, 17·1; H_2O, 4·6. $CuC_{12}H_{12}N_8,Cl_2H_2O$ requires Cu, 15·1; Cl, 16·9; H_2O, 4·3%).

The original solution containing hydrochloric acid was warmed and aqueous sodium hydroxide added to pH ~8. A pink precipitate of the inner *complex* appeared. This was centrifuged off while hot and the solid digested with hot water several times to remove unchanged ligand or cationic complex. The final residue was light brown (Found: Cu, 18·9; C, 45·0; H, 3·7; N, 34·0; Cl, 0. $CuC_{12}H_{10}N_8$ requires Cu, 19·3; C, 43·7; H, 3·1; N, 34·0%). Specimens which had not been washed thoroughly with hot water contained small amounts of chloride.

Complexes with other metals were prepared in the same way.

Nickel. The *complex sulphate* was pale blue (Found: Ni, 10·4; C, 39·3; H, 3·4; N, 29·9; SO_4, 17·4; H_2O, 0. $NiC_{12}H_{12}N_{12}{\cdot}SO_4$ requires Ni, 10·5; C, 38·8; H, 3·3; N, 30·2; SO_4, 17·2%).

Attempts to wash solid NiA_3Cl_2 to remove the excess of sodium chloride produced a colourless residue of ligand. All the chloride or iodide complexes of this ligand were very easily hydrolysed.

A *product*, NiR_2, formed a brown solid from slightly alkaline solution; when prepared from chloride solution it was light brown (Found: Ni, 17·9; C, 43·8; H, 3·0; N, 34·1. $NiC_{12}H_{10}N_8$ requires Ni, 18·1; C, 44·4; H, 3·1; N, 34·5%), but when prepared from sulphate, however, analyses for nickel were always high, and for ligand low, indicating hydrolysis; the solid was always much darker brown.

Cobalt. A *sulphate*, CoA_3SO_4, was pink (Found: Co, 10·4; C, 39·2; H, 3·3; N, 30·5; SO_4, 17·7. $CoC_{18}H_{18}N_{12}{\cdot}SO_4$ requires Co, 10·6; C, 38·8; H, 3·3; N, 30·2; SO_4, 17·2%).

A purple product, CoR_2, was obtained from alkaline solution but was impure (Found, for material prepared from sulphate: Co, 18·7; C, 42·7; H, 3·1; N, 33·2. Calc. for $CoC_{12}H_{10}N_8$: Co, 18·1; C, 44·3; H, 3·1; N, 34·5%). The remarks made for the nickel complex apply in this case also.

Ferrous iron. A yellow *product*, FeA_3SO_4, was precipitated from an almost colourless solution. It was easily hydrolysed and was washed with dilute sulphuric acid (unlike the other cation sulphates formed by this ligand) (Found: Fe, 9·9; C, 38·5; H, 3·4; N, 30·0; SO_4, 17·6. $FeC_{18}H_{18}N_{12}{\cdot}SO_4$ requires Fe, 10·1; C, 39·0; H, 3·3; N, 30·3; SO_4, 17·3%).

No neutral complex was isolated; although a pale green precipitate was obtained at pH 10 it became contaminated with ferric hydroxide in attempts to purify it.

No complex was obtained for ferric iron, any precipitate being ferric hydroxide.

DISCUSSION

Imidazole does not release a hydrogen ion when titrated with sodium hydroxide, nor does it in the presence of metal ions. This has been shown by Edsall *et al.*[10] to pH 8, and by Holmes and Morris-Jones [11] for a number of substituted imidazoles to much higher pH's. The lower pK of the conjugated ligands considered in this paper would make for easier

[10] Edsall, Felsenfeld, Goodman, and Gurd, *J. Amer. Chem. Soc.*, 1954, **76**, 3054.
[11] Holmes and Morris Jones, unpublished information.

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release of the imino-hydrogen but there is no evidence for this up to pH 11. In the presence of metal ions, however, the stability of the chelated system causes the pK of the imino-hydrogen to be lowered further and the hydrogen is released on titration with sodium hydroxide.

This results in the formation of two series of complexes, with both 4-2′-pyridylimidazole and 2,2′-bi-imidazolyl. Those from acid solution are the normal cationic complexes; those from slightly alkaline solution are inner complexes and non-electrolytes.

The cationic complexes formed by the pyridylimidazole resemble those of bipyridyl. Copper(II) forms a bis-complex; bivalent cobalt, nickel, and iron form tris-complexes. The last-named is deep red, like the corresponding bipyridyl complex, and has a molar extinction coefficient of almost 10^4 in aqueous solution. However, unlike in the bipyridyl case, heating the tris-complexes *in vacuo* at 140° causes no apparent change. Nor can copper(I) derivatives be made, directly or by simple reduction with hydrazine or hydroxylamine.

Similar complexes can, in general, be formed from 2,2′-bi-imidazolyl. However, although this ligand is about as basic as the pyridylimidazole its complexes are more easily hydrolysed. In particular, the halides proved difficult to purify. Approximate formation constants show that they are less stable, so this result is not unexpected. The iron(II) complex is not highly coloured and would probably be paramagnetic.

The systems will be discussed later in detail, together with other similar ones. The behaviour of the ligands now considered may give some support to Pauling's suggestion of imidazole ionisations in hæmoglobin; as has already been said, no such ionisation has been observed with complexes of imidazole itself [10] or with compounds such as histamine and related molecules with a second nitrogen atom which is aliphatic,[12] yet it becomes possible in the more highly conjugated systems discussed in this paper.

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[*Received, May* 23*rd*, 1961.]

[12] Holmes and Jones, *J.*, 1960, 2398.

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945. *Hydrogen Transfer. Part XIX.*[1] *Dehydrogenation of Substituted* 1,2-*Dihydronaphthalenes by Quinones, and the Correlation of Donor Reactivity with the Nature of Substituents.*

By L. M. JACKMAN and D. T. THOMPSON.

The stoicheiometry and kinetics of the dehydrogenation of a series of substituted 1,2-dihydronaphthalenes by tetrachloro-1,2-benzoquinone in 1,2-dichlorobenzene have been studied. A charge-transfer complex is formed between the reactants; the significance of this, and the degree of complex formation, are discussed. The rates have been correlated with σ and σ^+, and certain deviations from the straight-line plots have been shown to be due to a change in the principal site of attack in these cases from the 2- to the 1-position. The difference in ease of attack at the 1- and the 2-position of the dihydronaphthalene system has been assessed. The results are discussed in terms of the two-step ionic mechanism postulated in earlier papers. Syntheses of a number of new 1,2-dihydronaphthalenes are described.

IT has been shown (Part II [2]) that, in accord with the postulated two-step ionic mechanism, the reactivity of quinones is increased by the presence of electron-attracting

[1] Part XVIII, Braude, Hannah, and Linstead, *J.*, 1960, 3268.
[2] Braude, Jackman, and Linstead, *J.*, 1954, 3548.

substituents, and that there is a linear free-energy relation with oxidation–reduction potentials. In the first section of this paper an investigation into the kinetics of the dehydrogenation of a series of 6- and 7-substituted 1,2-dihydronaphthalenes by tetrachloro-1,2-benzoquinone is described, in which the effect of substituents on the rate of dehydrogenation is established; the second section describes the synthesis of a number of new 1,2-dihydronaphthalenes; and the third section contains the results of preparative dehydrogenations which establish the stoicheiometry of the class of reactions discussed in the first section.

Kinetic Studies.—All kinetic experiments were carried out with 1,2-dichlorobenzene as solvent; the rate of disappearance of quinone was measured by the spectroscopic technique " b " described in Part XI.[3] Each reaction was found to obey the second-order rate equation up to at least 80% completion (70% in the case of 1,2-dihydro-2,2-dimethylnaphthalene). However, it was observed that with many of the dihydronaphthalenes the initial optical density of the reaction system at 5700 Å was higher than that found for a solution of the same concentration of quinone alone in the solvent (Table 1). These results indicate that the quinone and the dihydronaphthalenes form

TABLE 1.

Initial extinction coefficients of 1,2-dihydronaphthalenes (0·0500M) and tetrachloro-1,2-benzoquinone (0·0100M) in 1,2-dichlorobenzene.

Subst. 1,2-dihydronaphthalene	Temp. range	E_0 (5700 Å) range	Subst. 1,2-dihydronaphthalene	Temp. range	E_0 (5700 Å) range
Control (0·01M-quinone) ...	23·0°	0·98	7-Methyl.....	36·8—55·3°	1·28—1·32
Parent compound	48·3—77·2°	0·98—1·03	6-Methyl.....	31·9—56·7	1·25—1·32
1,1-Dimethyl-.....	60·4—82·4	0·97—1·03	6-Acetamido-.....	36·1—61·9	1·17—1·25
2,2-Dimethyl-.....	88·0—114·8	0·94—1·00	7-Chloro-	68·2—90·5	0·94—0·98
7-Methoxy-.....	22·6—39·8	1·40—1·45	6-Chloro-	70·9—93·2	0·94—0·97
7-Methoxy-1,1-dimethyl- ...	27·4—42·4	1·10—1·17	6-Bromo-	71·0—93·1	0·92—0·95
6-Methoxy-	28·0—52·8	1·17—1·24	6-Nitro-	89·2—111·5	0·90—0·91
6-Methoxy-1,1-dimethyl- ...	55·9—73·9	1·05—1·12			

charge-transfer complexes and, as expected, the tendency to do so is most pronounced with the dihydronaphthalenes bearing electron-donating substituents. Complex formation between the reactants was not observed in previous investigations carried out with phenetole as solvent, presumably because the solvent itself forms a complex with the quinone (see below).

The initial formation of a charge-transfer complex between the reactants can be demonstrated by studying the kinetics at varying concentrations of reactants.[4] Second-order rate constants for the 1,2-dihydro-6-methylnaphthalene reaction have been determined at a series of concentrations of hydrocarbon (Fig. 1). Andrews and Keefer [4] have shown that when one of the reactants is present in excess the observed second-order rate constants ($k_{obs.}$) are related to the equilibrium constant (K) for complex formation and the rate constant (k_1 or k_2) of the rate-determining step by equations (3) and (4) (which are written here for an excess of donor), depending on whether the complex undergoes the product-forming reaction (1) or is an unreactive by-product (2), respectively.

$$Q + DHN \underset{(Fast)}{\overset{K}{\rightleftharpoons}} Q.DHN \xrightarrow[(Slow)]{k_1} Products \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$Q + DHN \xrightarrow[(Slow)]{k_2} Products \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$\begin{array}{l} {\scriptstyle (Fast)}\downarrow\uparrow{\scriptstyle K} \\ Q + DHN \end{array}$$

$$1/k_{obs.} = 1/k_1K + [DHN]/k_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$1/k_{obs.} = 1/k_2 + K[DHN]/k_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

[3] Braude, Jackman, Linstead, and Shannon, *J.*, 1960, 3116.
[4] Andrews and Keefer, *J. Amer. Chem. Soc.*, 1955, **77**, 6284.

K, k_1, and k_2 can be evaluated from the plot of $1/k_{obs.}$ against [DHN] (Fig. 1), which should have a constant slope in the region where the concentration of dihydronaphthalene is much greater than that of the quinone. Thus we have used Fig. 1 to give us the approximate values $k_1 = 0{\cdot}67 \times 10^{-2}$ sec.$^{-1}$ by equation (3), and $k_2 = 1{\cdot}2 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$ by equation (4); $K = 1{\cdot}8$ l. mole^{-1} by both equations.

Andrews and Keefer [4] also used the variation of initial optical densities with concentration of reactants as an independent means of evaluating the equilibrium constant.

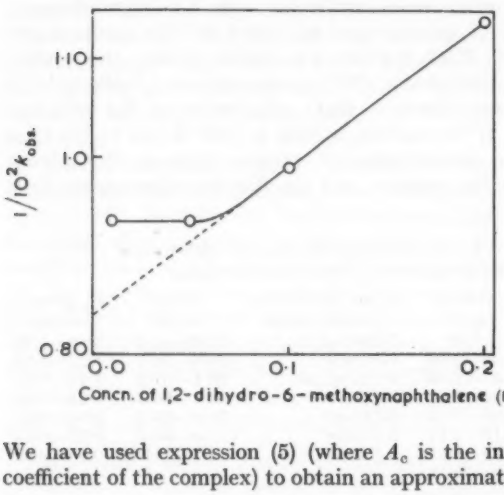

FIG. 1. Plot of $1/k_{obs.}$ against concentration of 1,2-dihydro-6-methylnaphthalene with 0·0100M-tetrachloro-1,2-benzoquinone.

We have used expression (5) (where A_c is the initial absorbance and ε_c the extinction coefficient of the complex) to obtain an approximate value

$$[Q]/A_c = (K\varepsilon_c)^{-1}\,(1/[DHN]) + 1/\varepsilon_c \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

of $K = 2$ l. mole^{-1}. It is seen that the two values of K are in reasonable agreement. It is not possible to distinguish between the paths represented by equations (1) and (2). In principle, values of k_2 (or k_1K) could be determined for the entire series of dihydronaphthalenes but in practice such experiments would require considerable quantities of materials, some of which are difficult to obtain. However, the results obtained for 1,2-dihydro-6-methylnaphthalene indicate that although $k_{obs.}$ determined at 0·05M-concentration of the hydrocarbon is lower than k_2 (or k_1K) the error introduced by equating the two is small. This error will probably be somewhat larger for the methoxy-derivatives but substantially smaller for those derivatives which have electron-withdrawing substituents. We have therefore determined $k_{obs.}$ at 0·05M-concentration for each member of the series and will use these values for comparing the relative reactivities of the dihydronaphthalenes. Table 2 gives values of observed second-order rate constants, $k_{obs.}$, at 25° and the related Arrhenius parameters $\Delta S^{\ddagger}$ and E_A.

The results can now be discussed in terms of the two-step ionic mechanism postulated in earlier papers.[2,3,5-8] If it is assumed that the rate-controlling hydride-ion abstraction occurs at the 2-position of the dihydronaphthalene, 6- and 7-substituents are respectively analogous to *meta*- and *para*-substituents in their electronic effects. Fig. 2 shows the Hammett plot based on $k_{obs.}$ at 25° and Jaffé's [9] σ-values. With the exceptions of 6-acetamido-1,2-dihydronaphthalene and 1,2-dihydro-6-methoxynaphthalene, a reasonable

[5] Braude, Jackman, and Linstead, *J.*, 1954, 3564.
[6] Barnard and Jackman, *J.*, 1960, 3110.
[7] Braude, Jackman, Linstead, and Lowe, *J.*, 1960, 3123.
[8] Braude, Jackman, Linstead, and Lowe, *J.*, 1960, 3133.
[9] Jaffé, *Chem. Rev.*, 1953, **53**, 191.

TABLE 2.

Arrhenius parameters and observed rate constants at 25°.

Subst. 1,2-dihydronaphthalene	$k_{obs.}$ (l. mole^{-1} sec.$^{-1}$)	$\Delta S_{25}^{\ddagger}$ (E.U.)	E_A (kcal. mole^{-1})
Parent compound	$1{\cdot}19 \pm 0{\cdot}08 \times 10^{-3}$	$30{\cdot}2 \pm 1{\cdot}5$	$13{\cdot}2 \pm 0{\cdot}4$
1,1-Dimethyl-	$7{\cdot}36 \pm 0{\cdot}84 \times 10^{-4}$	$31{\cdot}4 \pm 1{\cdot}9$	$14{\cdot}3 \pm 0{\cdot}5$
2,2-Dimethyl-	$3{\cdot}03 \pm 0{\cdot}15 \times 10^{-5}$	$28{\cdot}9 \pm 3{\cdot}5$	$15{\cdot}5 \pm 1{\cdot}0$
7-Methoxy	$2{\cdot}29 \pm 0{\cdot}10 \times 10^{-2}$	$30{\cdot}8 \pm 1{\cdot}4$	$10{\cdot}4 \pm 0{\cdot}4$
7-Methoxy-1,1-dimethyl-	$1{\cdot}43 \pm 0{\cdot}06 \times 10^{-2}$	$31{\cdot}4 \pm 0{\cdot}8$	$11{\cdot}9 \pm 0{\cdot}2$
6-Methoxy-	$9{\cdot}93 \pm 0{\cdot}33 \times 10^{-3}$	$31{\cdot}7 \pm 1{\cdot}4$	$11{\cdot}5 \pm 0{\cdot}4$
6-Methoxy-1,1-dimethyl-	$9{\cdot}73 \pm 0{\cdot}92 \times 10^{-4}$	$24{\cdot}9 \pm 1{\cdot}9$	$14{\cdot}9 \pm 0{\cdot}5$
7-Methyl-	$4{\cdot}47 \pm 0{\cdot}14 \times 10^{-3}$	$31{\cdot}0 \pm 1{\cdot}1$	$12{\cdot}2 \pm 0{\cdot}3$
6-Methyl-	$4{\cdot}06 \pm 0{\cdot}06 \times 10^{-3}$	$29{\cdot}5 \pm 0{\cdot}4$	$12{\cdot}1 \pm 0{\cdot}1$
6-Acetamido-	$3{\cdot}31 \pm 0{\cdot}15 \times 10^{-3}$	$32{\cdot}8 \pm 1{\cdot}1$	$11{\cdot}8 \pm 0{\cdot}3$
7-Chloro-	$4{\cdot}37 \pm 0{\cdot}12 \times 10^{-4}$	$29{\cdot}8 \pm 0{\cdot}6$	$13{\cdot}9 \pm 0{\cdot}1$
6-Chloro-	$2{\cdot}81 \pm 0{\cdot}22 \times 10^{-4}$	$28{\cdot}0 \pm 1{\cdot}2$	$14{\cdot}6 \pm 0{\cdot}3$
6-Bromo-	$2{\cdot}87 \pm 0{\cdot}19 \times 10^{-4}$	$27{\cdot}8 \pm 0{\cdot}8$	$14{\cdot}8 \pm 0{\cdot}2$
6-Nitro-	$5{\cdot}13 \pm 0{\cdot}95 \times 10^{-5}$	$27{\cdot}8 \pm 2{\cdot}0$	$15{\cdot}8 \pm 0{\cdot}5$

correlation is obtained. When the σ^+-values, determined by Brown and Okamoto,[11] are used instead of σ (Fig. 3) the only points falling a significant distance from the plot are those arising from the experiments with compounds having electron-donating

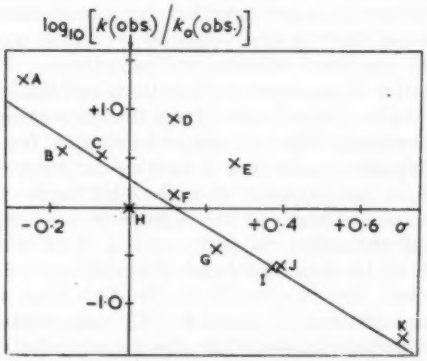

FIG. 2. Hammett plot based on Jaffé's σ-values.[9] (σ for *m*-acetamido was determined by McDaniel and Brown.[10])

A, 7-MeO. B, 7-Me. C, 6-Me. D, 6-MeO. E, 6-NHAc. F, 6-MeO-1,1-Me_2 (corr.). G, 7-Cl. H, Unsubst. I, 6-Cl. J, 6-Br. K, 6-NO_2.

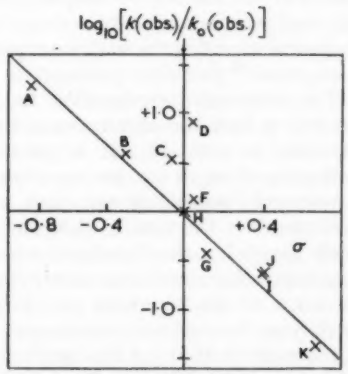

FIG. 3. ρ–σ^+ Correlation based on Brown and Okamoto's σ^+ values.[11] Key as for Fig. 2.

6-substituents (methoxy and methyl). That these deviations are not due to the assumption that $k_{obs.}$ is equal to k_2 (or k_1K) can be demonstrated by the inclusion of points corresponding to the correct value of k_2 (or k_1K) for the 6-methyl compound. Two possible explanations for the observed deviations will now be considered.

If the reaction follows scheme (1), so that $k_{obs.} \approx k_1K$, either or both steps could determine the relative reactivities used in the σ and σ^+ correlations. If K is the dominant term it may be incorrect to assign *meta*- and *para*-substituent constants to the 6- and the 7-position, respectively. Thus, if complex formation is merely determined by the activation of the aromatic ring, the position of the substituent would be unimportant. If *para*-substituent constants are used for both the 6- and the 7-substituted 1,2-dihydronaphthalenes, there are no longer any deviations as great as those observed for the

[10] McDaniel and Brown, *J. Org. Chem.*, 1958, **23**, 420.
[11] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979.

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6-methoxy-substituent in the previous plots (Figs. 2 and 3), but the overall correlations are not as good as those in Figs. 2 and 3.

For the 1,2-dihydro-6-methylnaphthalene reaction, the values of K and E_0 at 40° have been used to afford the magnitude of the molecular extinction coefficient (ε_c) of the complex. This value for ε_c was then used, together with the initial extinction coefficients at various temperatures, in calculating an approximate value of —0·6 kcal. mole^{-1} for the heat of formation of the complex. If anything, the optical density for the 6-nitro-compound decreases with increasing temperature, so that even for this compound the heat of formation of the complex is less than, or equal to, zero. The difference in the heat of formation of $>$0·6 kcal. mole^{-1} for complexes with the 6-methyl and the 6-nitro-compound is substantially less than that (3·6 kcal. mole^{-1}) between their activation energies for dehydrogenation. The former value is of the same order as that (0—1·5 kcal. mole^{-1}) found for the heats of formation of complexes between tetrachloro-1,4-benzoquinone and a series of *meta*- and *para*-substituted styrenes, ranging from the *p*-methoxy- to the *m*-chloro-derivatives, by Walling *et al.*[12] It is therefore unlikely that complex formation can play a major rôle in determining the sensitivity of the reaction to substituent effects. Further, it is probable that complex-formation involves the isolated double bond rather than the aromatic ring. If initial extinction coefficients (Table 1) can be regarded as an approximate measure of complex formation, it is seen that the 6-methoxy-compound forms a complex less readily than does the 7-derivative, suggesting that the isolated double bond is in fact the site of complex formation and that we were originally correct in using *meta*- and *para*-substituent constants for the 6- and the 7-substituents, respectively. The conclusion regarding the site of complex formation is consistent with Andrews and Keefer's observations[13] that silver cations form a more stable complex with styrene than with anisole.

The alternative explanation for the anomalous effect of electron-donating 6-substituents is that the initial assumption of exclusive removal of a hydride ion from the 2-position is incorrect. It is possible that in the presence of such substituents the mechanism changes to one involving predominant attack at the 1-position. In order to test this possibility we have examined the effect of a 6- and a 7-methoxy-substituent on the rate of dehydrogenation of 1,2-dihydro-1,1-dimethylnaphthalene in which attack at the 1-position cannot occur. The results (Table 2) show that the 6-methoxy-substituent is no longer effective in activating the reaction. The rate constant for attack at the 2-position of 1,2-dihydro-7-methoxynaphthalene can be estimated by multiplying the observed rate constant for 1,2-dihydro-7-methoxy-1,1-dimethylnaphthalene by the ratio (1·62 : 1) of the rate constants for 1,2-dihydronaphthalene and 1,2-dihydro-1,1-dimethylnaphthalene. The value thus obtained for 1,2-dihydro-7-methoxynaphthalene is $2{\cdot}32 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$, in excellent agreement with the observed value ($2{\cdot}29 \times 10^{-2}$ l. mole^{-1} sec.$^{-1}$). A similar calculation gives the rate constant for 1,2-dihydro-6-methoxynaphthalene as $1{\cdot}58 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$ which is substantially lower than the observed value ($9{\cdot}93 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$); when assigned σ- and σ^+-values for the *m*-methoxy-substituent these results give points which fall close to the plots (Figs. 2 and 3) obtained from 7-substituents and electron-attracting 6-substituents. There is little doubt, therefore, that the anomalous effect of electron-donating 6-substituents is due to a change from the 2- to the 1-position as the principal site of hydride ion abstraction.

The relative rate constants for attack at the 1- and the 2-position of 1,2-dihydronaphthalene itself can be estimated from the ratio of the rate constants for reaction with 1,2-dihydro-2,2-dimethyl- and 1,2-dihydro-1,1-dimethyl-naphthalene, and it is seen that attack at the 2-position is favoured by a factor of *ca.* 24. This result confirms earlier conclusions[7,8] and reflects the relative stabilities of the 1- and the 2-naphthalenium ion.[6] In the presence of a 6-methoxy-substituent the rate constant for attack at the 2-position is reduced to 0·19 times that for attack at the 1-position.

[12] Walling, Briggs, Wolfstern, and Mayo, *J. Amer. Chem. Soc.*, 1948, **70**, 1537.
[13] Andrews and Keefer, *J. Amer. Chem. Soc.*, 1949, **71**, 3644; 1950, **72**, 3113, 5034.

The ρ-value observed for the reaction represents an upper limit for the sensitivity of hydride ion abstraction to the nature of substituents in the donor, because if mechanism (1) operates the observed value of ρ will be the sum of the ρ-values for the two steps and these will both be negative. Our ρ-value (−2·5) would be consistent with an ionic nature of mechanism (2) as it is of the same magnitude as that (−2·6) found [9] for the solvolysis of triphenylmethyl chlorides,[14] an ionic reaction having comparable activation energy (12·5 kcal. mole^{-1} for the *p*-methyl to 16·7 kcal. mole^{-1} for the *p*-nitro-derivative).

At 77°, the rate constant for the reaction of 1,2-dihydronaphthalene in phenetole [8] is smaller by a factor of 3·1 times that observed here for reaction in 1,2-dichlorobenzene. However, the activation energy of the reaction in phenetole is 2·2 kcal. mole^{-1} greater than that for the reaction in 1,2-dichlorobenzene and the difference is doubtless due to the fact that the quinone forms complexes strongly with the former solvent. The solvent–quinone complex-formation can be clearly demonstrated by light-absorption measurements. At 25°, the optical density at 6050 Å of a 0·01M-solution of the quinone is 0·9 in phenetole compared with 0·2 in 1,2-dichlorobenzene.

The Preparation of 6- *and* 7-*Substituted* 1,2-*Dihydronaphthalenes.*—The most convenient synthetic approach involved preparation of the appropriate 1-tetralone, the majority of which were obtained by cyclisation in anhydrous hydrofluoric acid of the corresponding substituted phenylbutyric acid, or by oxidation of the appropriately substituted tetralin. Schroeter's method [15] was used to prepare 7-nitro-1-tetralone from 1-tetralone. Selective reduction [16] of the nitro-group of this ketone, and acetylation of the product gave 7-acetamido-1-tetralone. The 1-tetralones were reduced with potassium borohydride or aluminium isopropoxide,[17] and the resulting 1-tetralols dehydrated to give the 1,2-dihydronaphthalene.

1,2-Dihydro-1,1-dimethylnaphthalene was prepared by the method described earlier,[7,8] except that we carried out the cyclodehydration of 1,1-dimethyl-4-phenylbutan-1-ol to 1,1-dimethyltetralin very effectively in anhydrous hydrofluoric acid. 6- and 7-Methoxy-1,1-dimethyltetralin were obtained by similar cyclodehydration of 4-*m*- and 4-*p*-methoxyphenyl-1,1-dimethylbutan-1-ol, respectively. These alcohols were obtained from acetone and the Grignard compound formed from the appropriate 1-bromo-3-methoxyphenylpropane. However, neither of these last two cyclodehydrations can be regarded as unambiguous. The *meta*-derivative can in principle cyclise in either the *ortho*- or the *para*-positions by the Ar_2-6 mechanism,[18] although for steric reasons the latter is the more likely. The product appeared to be homogeneous on vapour-phase chromatography and its nuclear magnetic resonance spectrum showed it to be a 1,3,4- rather than a 1,2,3-trisubstituted benzene since one proton resonance did not exhibit an *ortho*-coupling. There can therefore be no doubt that this compound is 6-methoxy-1,1-dimethyltetralin. Cyclisation of the *para*-alcohol probably takes place by an Ar_1-5 mechanism [18] involving the spiro-intermediate (I), rather than direct substitution at the positions *meta* to the methoxy-substituent. The subsequent rearrangement of (I) could yield either 6- or 7-methoxytetralin although preferential migration of the more heavily substituted carbon is expected.[18] Again the product was homogeneous and it had an infrared spectrum different from that for 6-methoxy-1,1-dimethyltetralin; it must therefore be the 7-methoxy-isomer. Support for the assigned structures of these two tetralins was obtained when the conversion of these two isomers into the 1,2-dihydronaphthalenes was attempted. The 6-isomer was converted into the 4-bromo-derivative by *N*-bromosuccinimide,[8] and subsequently dehydrobrominated [8] to 1,2-dihydro-6-methoxy-1,1-dimethylnaphthalene. In contrast, bromination of the 7-methoxy-compound was followed

[14] Nixon and Branch, *J. Amer. Chem. Soc.*, 1936, **58**, 492.
[15] Schroeter, *Ber.*, 1930, **63**, 1308.
[16] Veselý and Stürsa, *Coll. Czech. Chem. Comm.*, 1933, **5**, 170, 174.
[17] Macbeth and Mills, *J.*, 1949, 2646.
[18] Winstein, Heck, Lapporte, and Baird, *Experientia*, 1956, **12**, 138.

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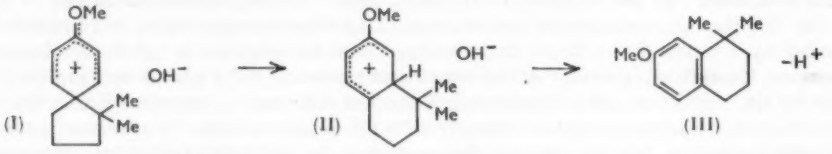
by spontaneous dehydrobromination, consistently with the ready loss of bromide ion from a benzylic position *para* to a methoxy-substituent. The desired dihydronaphthalene was obtained by oxidation of the tetralin with chromic–acetic acid, and the product was purified by means of its 2,4-dinitrophenylhydrazone. Reduction of the regenerated ketone and dehydration of the resulting tetralol gave 1,2-dihydro-7-methoxy-1,1-dimethylnaphthalene.



1,2-Dihydro-2,2-dimethylnaphthalene was prepared by a combination of the methods described above. 3-Benzoylpivalic acid was reduced by the Clemmensen method and the resulting αα-dimethyl-γ-phenylbutyric acid cyclised by the hydrofluoric acid method. Clemmensen reduction of the 2,2-dimethyl-1-tetralone gave the corresponding tetralin, oxidation of which as above afforded a mixture of 2,2- and 3,3-dimethyl-1-tetralone. Only the latter readily formed a 2,4-dinitrophenylhydrazone, providing a convenient method of separation. Regeneration of the ketone followed by reduction and dehydration gave 1,2-dihydro-2,2-dimethylnaphthalene.

1,2-Dihydronaphthalene itself was prepared by Straus and Lemmel's method.[19]

Preparative Dehydrogenations.—In order to check the stoicheiometry of the reactions investigated kinetically, preparative dehydrogenations were carried out between each of the 1,2-dihydronaphthalenes and tetrachloro-1,2-benzoquinone. Quantitative recovery of naphthalenes when 1,2-dichlorobenzene was used as a solvent was not feasible and benzene was used instead. The naphthalene was usually obtained in high yield and shown to be of high purity by melting point, mixed melting point, or ultraviolet-light absorption (Table 3), but some cases require comment. With the 7-methyl and the 7-chloro-compound only 50 mg. of the dihydronaphthalenes were available, so that the yields were poor, but the identity and purity of the naphthalenes were established by infrared spectroscopy.

TABLE 3.

Preparative dehydrogenation of 1,2-dihydronaphthalenes by tetrachloro-1,2-benzoquinone.

Subst. 1,2-dihydronaphthalene	Recovered * crude naphthalene	Purity of naphthalene (U.V.)	Overall yield (%) of naphthalene
7-Methoxy-	99%		
6-Methoxy-	100	99%	99
7-Methyl-	83		
6-Methyl-	81	95	77
6-Acetamido-	100	89	89
7-Chloro-	52		
6-Chloro-	89	87	78
6-Bromo-	87	91	79
6-Nitro-	99	94	93
7-Methoxy-1,1-dimethyl-	95		
6-Methoxy-1,1-dimethyl-	47		
2,2-Dimethyl-	48		

* When pure naphthalene was put through the same working-up procedure it was recovered in 68% yield.

Dehydrogenation of 1,2-dihydro-6-methoxy-1,1-dimethylnaphthalene gave a crude product, whose ultraviolet absorption was consistent with what can be predicted from the

[19] Straus and Lemmel, *Ber.*, 1921, **54**, *B*, 25.

spectra of naphthalene,[20] 1,2-dimethylnaphthalene,[8] and 2-methoxynaphthalene for the unknown 6-methoxy-1,2-dimethylnaphthalene. Similarly, the 1,2-dihydro-7-methoxy-1,1-dimethylnaphthalene gave a crude product containing naphthalenoid material.

Dehydrogenation of 1,2-dihydro-2,2-dimethylnaphthalene gave a poor recovery of hydrocarbon which contained some 1,2-dimethylnaphthalene but was mainly unchanged dihydronaphthalene.

Dehydrogenation of 1,2-dihydronaphthalene [8] and 1,2-dihydro-1,1-dimethylnaphthalene [8] has been described previously.

In one case (1,2-dihydro-6-methylnaphthalene) tetrachlorocatechol was isolated.

Experimental

Microanalyses were carried out in the Microanalytical Laboratory (Miss J. Cuckney), and ultraviolet and infrared spectra were measured in the Spectrographic Laboratory (Mrs. A. I. Boston and Dr. R. L. Erskine) of this Department. Ultraviolet spectra refer to ethanol solutions. Nuclear magnetic resonance data, quoted as τ values,[21] were obtained with a Varian Associates V-4300 spectrometer and a 56·445 Mc/sec. oscillator at 21°. Spectra were calibrated by the side-band technique.

Kinetic Experiments.—Materials. Pure 1,2-dichlorobenzene was distilled from sodium and had b. p. 177—178°/746 mm., n_D^{25} 1·5480. Tetrachloro-1,2-benzoquinone,[22] supplied by Messrs. Hopkin and Williams Ltd., was purified by sublimation.

Reaction rates. The rates were determined by following spectrometrically the disappearance of the quinone. E_0 values were determined by graphical extrapolation to zero time. The experimental method was method " b " described in Part XI.[3] Values of $k_{obs.}$ were calculated from the normal second-order rate equation. The Arrhenius parameters were computed by the method of least squares, and their precision (standard deviations) by the equations set out in a previous paper.[3] Values of $k_{obs.}$ at 25° were obtained by least-squares extrapolation and the method of least squares was also used to obtain the ρ values:

$$\text{For Fig. 2, } \rho = -2{\cdot}5 \pm 0{\cdot}2, \; y \text{ intercept} = 0{\cdot}3 \pm 0{\cdot}1.$$

$$\text{Fig. 3, } \rho = -1{\cdot}8 \pm 0{\cdot}1, \; y \text{ intercept} = 0{\cdot}04 \pm 0{\cdot}05.$$

Individual runs. Two representative runs are recorded in full. Following these is a summary of rate constants for all the runs. Unless otherwise stated, the initial concentration of quinone was 0·0100M, and that of the 1,2-dihydronaphthalene 0·0500M. 1,2-Dichlorobenzene was the only solvent used.

(1) (a) *Stability of tetrachloro-1,2-benzoquinone in 1,2-dichlorobenzene at* 117°.

t (min.)	0	80	140	200	335
E (5700 Å)	0·767	0·764	0·761	0·759	0·755

(b) *Variation of quinone absorbance with temperature.*

Temp.	22°	36·2°	50·3°	74·8°	97·1°
E (5700 Å)	0·98	0·96	0·93	0·86	0·81

(2) *1,2-Dihydro-6-methoxynaphthalene at* 47·3°.

t (min.)	0	8	9	10	11	12	13	14	15
E (5700 Å)	1·23	0·499	0·448	0·407	0·363	0·328	0·297	0·268	0·241
$10^3 k_{obs.}$ (l. mole^{-1} sec.$^{-1}$)	—	4·03	4·06	4·00	4·06	4·03	4·03	4·03	4·04

(3) *1,2-Dihydro-6-nitronaphthalene at* 108°.

t (min.)	0	12	15	17	19	20	24	25	28	31	32
E (5700 Å)	0·90	0·496	0·430	0·399	0·367	0·350	0·298	0·287	0·251	0·222	0·211
$10^3 k_{obs.}$ (l. mole^{-1} sec.$^{-1}$)	—	1·74	1·75	1·70	1·70	1·70	1·67	1·67	1·67	1·66	1·67

[20] Friedel and Orchin, " Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, 1951.
[21] Tiers, *J. Phys. Chem.*, 1958, **62**, 1151.
[22] Braude, Brook, and Linstead, *J.*, 1954, 3569.

Summary of rate constants.

(The units for rate constants are l. mole^{-1} sec.$^{-1}$.)

1,2-Dihydronaphthalene						
Temp.	48·3°	53·5°	57·8°	62·7°	67·5°	77·2°
$10^3k_{obs.}$	0·610	0·780	1·09	1·42	1·98	3·21

1,2-Dihydro-7-methoxynaphthalene						
Temp.	22·0°	23·4°	23·6°	28·5°	32·0°	34·8°	39·8°
$10^3k_{obs.}$	1·97	2·07	2·10	2·77	3·27	3·92	5·46

1,2-Dihydro-6-methoxynaphthalene						
Temp.	28·0°	34·2°	38·5°	43·4°	47·3°	52·8°
$10^3k_{obs.}$	1·18	1·77	2·30	3·07	4·04	4·96

1,2-Dihydro-7-methylnaphthalene						
Temp.	36·8°	42·4°	45·2°	50·6°	54·6°	55·3°
$10^3k_{obs.}$	0·981	1·39	1·61	2·27	2·81	3·06

1,2-Dihydro-6-methylnaphthalene						
Temp.	31·9°	35·6°	41·4°	45·9°	51·8°	56·7°
$10^3k_{obs.}$	0·643	0·816	1·20	1·53	2·23	2·86

6-Acetamido-1,2-dihydronaphthalene						
Temp.	36·1°	41·3°	45·8°	51·7°	56·0°	61·5°	61·9°
$10^3k_{obs.}$	0·667	0·955	1·24	1·63	2·13	2·84	3·14

7-Chloro-1,2-dihydronaphthalene						
Temp.	68·2°	72·7°	79·5°	82·5°	89·2°	90·5°
$10^3k_{obs.}$	0·847	1·12	1·64	1·94	2·77	3·03

6-Chloro-1,2-dihydronaphthalene						
Temp.	70·9°	75·3°	79·0°	83·9°	88·9°	93·2°
$10^3k_{obs.}$	0·761	0·987	1·23	1·60	2·16	2·84

6-Bromo-1,2-dihydronaphthalene						
Temp.	71·0°	75·6°	79·7°	84·1°	89·4°	93·1°
$10^3k_{obs.}$	0·816	1·09	1·37	1·74	2·42	3·05

1,2-Dihydro-6-nitronaphthalene						
Temp.	89·2°	93·7°	96·9°	102·2°	108°	111·5°
$10^3k_{obs.}$	0·597	0·704	0·897	1·22	1·69	2·04

1,2-Dihydro-1,1-dimethylnaphthalene						
Temp.	60·4°	64·4°	67·4°	73·2°	77·4°	82·4°
$10^3k_{obs.}$	0·960	1·19	1·52	2·11	2·56	3·74

1,2-Dihydro-2,2-dimethylnaphthalene						
Temp.	88·0°	92·8°	97·9°	104·5°	109·2°	114·8°
$10^3k_{obs.}$	0·260	0·420	0·545	0·779	0·945	1·23

1,2-Dihydro-7-methoxy-1,1-dimethylnaphthalene				
Temp.	27·4°	34·1°	37·5°	42·4°
$10^3k_{obs.}$	1·49	2·44	2·80	3·90

1,2-Dihydro-6-methoxy-1,1-dimethylnaphthalene					
Temp.	55·9°	57·1°	60·5°	64·5°	69·6°	73·9°
$10^3k_{obs.}$	1·06	1·17	1·44	1·83	2·59	3·31

Determination of the Heat of Formation of the Complex with 1,2-*Dihydro*-6-*methylnaphthalene.*—The initial concentration of hydrocarbon (DHN) was varied as indicated below. Kinetic runs were carried out at two temperatures in each case and $k_{obs.}$ at 40° was evaluated by interpolation of the Arrhenius plots. The initial concentration of quinone was always 0·0100M.

[DHN]	0·0100M	0·0100M	0·100M	0·100M	0·200M	0·200M
Temp.	36·7°	47·0°	36·8°	46·2°	36·4°	43·1°
$10^3k_{obs.}$ (l. mole^{-1} sec.$^{-1}$)	0·852	1·65	0·817	1·48	0·694	1·07

At 0·05M-hydrocarbon, E_0 (31·9°) = 1·32, E_0 (56·7°) = 1·25, and (by interpolation) E_0 (40°) = 1·29. ε_Q can be calculated at each temperature from (1b) above.

$$K = [Q\,.\,DHN]/[Q][DHN] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$[Q] = 0{\cdot}01 - [Q\,.\,DHN] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$E = \varepsilon_Q[Q] + \varepsilon_C[Q\,.\,DHN] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

$$(\ln K_2 - \ln K_1) = -\Delta H/\boldsymbol{R}(1/T_1 - 1/T_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

The value $K = 1{\cdot}8$ l. mole^{-1} found above, together with equations (6) and (7) can be used to give the initial concentration of complex as 8×10^{-4}M at 40°. Substitution in equation (7) gives $\varepsilon_C = 520$. If it is assumed that ε_C is independent of temperature (ΔH will be numerically smaller if a correction for solvent expansion is applied), equations (6) and (8) give $K_{31\cdot9} = 1{\cdot}84$ and $K_{56\cdot7} = 1{\cdot}70$ l. mole^{-1}, and by equation (9) $\Delta H = 0{\cdot}6$ kcal. mole^{-1}.

Preparation of 6- *and* 7-*Substituted* 1-*Tetralones.*—7-Methoxy-,[23] 7-chloro-,[24] and 7-bromo-1-tetralone [25] were prepared by recorded methods.

γ-*p*-Tolylbutyric acid [26] in anhydrous hydrofluoric acid (200 ml.) was left in a Polythene

[23] Haworth and Sheldrick, *J.*, 1934, 1950.
[24] Koo, *J. Amer. Chem. Soc.*, 1953, **75**, 1891.
[25] Fieser and Seligman, *J. Amer. Chem. Soc.*, 1938, **60**, 170.
[26] Fieser and Dunn, *J. Amer. Chem. Soc.*, 1936, **58**, 572.

beaker for 46 hr., then poured into an excess of dilute aqueous sodium carbonate and extracted with ether. This gave 7-methyl-1-tetralone (19·2 g., 70%) as prisms, m. p. 31—33° (lit.,[27] m. p. 31—33°).

Similar treatment of γ-phenylbutyric acid [28] (38·5 g.) with anhydrous hydrofluoric acid (250 ml.) for 40 hr. furnished 1-tetralone (34 g., 99%), n_D^{20} 1·5713 (lit.,[29] n_D^{20} 1·5693).

7-Nitro-1-tetralone was prepared by a modification of Schroeter's method.[15] The reaction was conducted at the lowest temperature at which the mixture remained liquid. Crystallisation of the product from light petroleum (b. p. 60—80°) afforded 7-nitro-1-tetralone (31%) as needles, m. p. 105—106° (lit.,[15] m. p. 106°).

7-Amino-1-tetralone [16] with acetic anhydride gave 7-acetamido-1-tetralone, prisms, m. p. 164—166°.

1,2-Dihydro-6-methylnaphthalene (6·3 g.; see below), ethanol (10 ml.), and Adams platinum oxide (28 mg.) were shaken in hydrogen at 21°/758·5 mm. until no more hydrogen was taken up (45 min.) (1026 ml. absorbed; theor. 1055 ml.). Filtration and removal of the solvent afforded 6-methyltetralin (6·1 g., 96%), $n_D^{22·5}$ 1·5366 (lit.,[30] n_D^{20} 1·5357).

6-Methoxy- [31] and 6-chloro-tetralin [32] were prepared by known methods.

6-Methoxy-, 6-methyl-, and 6-chloro-1-tetralone were prepared by the general method here described for 6-methyl-1-tetralone:

Chromium trioxide (6·7 g.) in water (3 ml.) and acetic acid (19 ml.) was added dropwise at 5—11° with stirring to 6-methyltetralin (6·1 g.) in acetic aid (38 ml.) during 1 hr. The solution was stirred at 0—5° for a further 3 hr. and left at room temperature for 3 days, then diluted with water (1 l.) and extracted with pentane (5 × 100 ml.). The combined extracts were washed with 2N-sodium carbonate (150 ml.). Removal of solvent from the dried ($MgSO_4$) extracts and distillation through a short Vigreux column gave impure 6-methyltetralin (2·1 g., 34%), b. p. 64—80°/1·2 mm., $n_D^{22·5}$ 1·5365—1·5453, and impure 6-methyl-1-tetralone (2·5 g., 33%), b. p. 98—104°/1·2 mm., $n_D^{22·5}$ 1·5619—1·5677. The crude ketone was treated with semicarbazide hydrochloride (5 g.) and sodium acetate (7·5 g.) in aqueous ethanol, and the *6-methyl-1-tetralone-semicarbazone* recrystallised from ethanol and from methanol, giving prisms (1·0 g., 30%), m. p. 238—239° (Found: C, 66·0; H, 7·0; N, 19·4. $C_{12}H_{15}N_3O$ requires C, 66·3; H, 7·0; N, 19·3%). A suspension of the semicarbazone (0·9 g.) and phthalic anhydride (2·5 g.) in water (50 ml.) was steam-distilled and 6-methyl-1-tetralone, n_D^{22} 1·557, was isolated by ether extraction of the distillate. This ketone was used in the next stage.

Oxidation of 6-methoxytetralin gave a crude solid product, m. p. 62—73°, recrystallisation (seven times from aqueous ethanol) of which afforded pure 6-methoxy-1-tetralone as needles, m. p. 75—78° (lit.,[31] m. p. 77·5°).

6-Chloro-1-tetralone semicarbazone was obtained as plates, m. p. 231—232° (Found: C, 55·6; H, 5·3; Cl, 14·6; N, 17·6. $C_{11}H_{12}ClN_3O$ requires C, 55·6; H, 5·1; Cl, 14·9; N, 17·7%).

Preparation of 6- and 7-Substituted 1,2-Dihydronaphthalenes.—Preparations of the 6- and the 7-methoxy-compounds were carried out by the method here described for the 6-methoxy-isomer.

The 6- [33] and the 7-methyl compound were prepared similarly except that the tetralols were dehydrated at 190° with potassium hydrogen sulphate.

Potassium borohydride (1·5 g.), 7-methoxy-1-tetralone (3·0 g.), and methanol (50 ml.) were refluxed for 3 hr. After cooling, the mixture was treated with concentrated hydrochloric acid (25 ml.). The resulting suspension was filtered and the methanol removed from the filtrate. The residue was extracted with ether (3 × 25 ml.), and the combined extracts were washed successively with 2N-sodium carbonate (30 ml.) and water (30 ml.). Removal of ether from the dried ($MgSO_4$) solution gave an oil which on distillation afforded 1,2-dihydro-6-methoxynaphthalene (1·8 g., 64%).

Potassium borohydride (2·5 g.), 7-acetamido-1-tetralone (3·3 g.), and methanol (50 ml.) were refluxed for 3 hr. On cooling, concentrated hydrochloric acid was added, and the resulting suspension filtered. Removal of the methanol left a brown solution, which was diluted with

[27] Newman, *J. Amer. Chem. Soc.*, 1940, **62**, 1683.
[28] Martin, *Org. Synth.*, Coll. Vol. II, p. 499.
[29] Linstead and Michaelis, *J.*, 1940, 1134.
[30] Mair and Streiff, *J. Res. Nat. Bur. Stand.*, 1941, **27**, 343.
[31] Burnop, Elliot, and Linstead, *J.*, 1940, 727.
[32] Schroeter, *Ber.*, 1938, **71**, 1040.
[33] Wenham and Whitehurst, *J.*, 1957, 4037.

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water (200 ml.). Acetic anhydride (3·0 ml.) was added with stirring to this brown solution of 6-amino-1,2-dihydronaphthalene hydrochloride. As soon as the mixture became homogeneous, sodium acetate (100 g.) in water (100 ml.) was added, and stirring continued for 15 min. The product was extracted with ether (100 ml., 2 × 25 ml.). The combined ether extracts were washed with 2N-sodium carbonate (75 ml.) and with water (50 ml.). Removal of ether from the dried ($MgSO_4$) extracts afforded a residue (3·0 g., 100%), m. p. 65—72°, which on recrystallisation from light petroleum (b. p. 60—80°) gave 6-acetamido-1,2-dihydronaphthalene as needles.

The 7-chloro-, 6-chloro-, 6-bromo-, and 6-nitro-compounds were prepared by the method here described for the 6-bromo-compound, except that the 6-nitro-compound was obtained from its tetralol by another method.

7-Bromo-1-tetralone (2·4 g.) in absolute propan-2-ol (25 ml.) was added dropwise during 2 hr. to aluminium isopropoxide (2·4 g.; b. p. 110—125°/1·5 mm.) in boiling absolute propan-2-ol (30 ml.) in a flask fitted with a 6″ Stedman column attached to a total condensation, variable-take-off distillation head. The 7-bromo-1-tetralone solution was warmed with a hot-air blower to prevent crystallisation, and the bath around the reaction vessel was maintained at *ca.* 140° so that the acetone formed passed immediately into the Stedman column. Propan-2-ol was removed slowly through the column and tested periodically for acetone. The volume of the solution was kept constant by the addition of more propan-2-ol. After 4 hr. the acetone test was negative, and the mixture was refluxed for 30 min. The propanol was removed under reduced pressure, the residue was cooled in ice-water, and ice-cold 2N-hydrochloric acid (50 ml.) was added. The liberated oil was extracted with ether and the combined extracts (100 ml.) were washed successively with water (30 ml.), N-hydrochloric acid (2 × 12·5 ml.), sodium hydrogen sulphite solution (2 g. in 10 ml.), and water (25 ml.). Removal of ether from the dried ($MgSO_4$) extracts left crude 7-bromo-1-tetralol which readily decomposed on distillation from potassium hydrogen sulphate into 6-bromo-1,2-dihydronaphthalene (1·71 g., 77%) and water.

7-Nitro-1-tetralol, formed in 99% yield by the above method, recrystallised from light petroleum (b. p. 60—80°) as needles, m. p. 109° (lit.,[34] m. p. 109°).

7-Nitro-1-tetralol, toluene-*p*-sulphonic acid (0·5 g.), and glacial acetic acid (60 ml.) were refluxed for 4½ hr., then diluted with water (1·5 l.) and extracted with ether (150 ml., 5 × 100 ml.). The combined ether extracts were washed with 2N-sodium carbonate (100 ml.) and with water (100 ml.). After removal of ether from the dried ($MgSO_4$) extracts, the residue was twice distilled, to give 1,2-dihydro-6-nitronaphthalene (1·8 g., 67%), m. p. 36°.

Synthesis of 1,2-*Dihydro*-1,1-*dimethylnaphthalene*.—(i) 1,1-*Dimethyltetralin*. Anhydrous hydrofluoric acid (100 ml.) was added to 1,1-dimethyl-4-phenylbutan-1-ol [7] (12·8 g.) and the resulting deep-red solution left for 3 days in a closed Polythene bottle. The solution was poured into a Polythene beaker and most of the acid allowed to evaporate. The residue was poured into an excess of aqueous sodium carbonate, and the product extracted with ether (300 ml.). This gave 1,1-dimethyltetralin (7·2 g., 62%), b. p. 56—62°/0·8 mm., n_D^{17} 1·5275 (lit.,[7] b. p. 40°/0·04 mm., n_D^{22} 1·5270).

(ii) 1,2-*Dihydro*-1,1-*dimethylnaphthalene*. This compound was prepared by the method described in Part XIII.[6]

Synthesis of 1,2-*Dihydro*-2,2-*dimethylnaphthalene*.—(i) 2,2-*Dimethyl*-1-*tetralone*. Cyclisation of γ-phenyl-αα-dimethylbutyric acid [35] by the hydrofluoric acid method furnished the tetralone, $n_D^{20·5}$ 1·5428 (lit.,[36] n_D^{25} 1·5414), in theoretical yield. When this ketone was treated with Brady's reagent, no precipitation occurred until 60 min. had elapsed.

(ii) 2,2-*Dimethyltetralin*. Amalgamated zinc (from 120 g. of zinc wool), water (70 ml.), concentrated hydrochloric acid (180 ml.), 2,2-dimethyl-1-tetralone (13·5 g.), and toluene (70 ml.) were refluxed for 15 hr. A further quantity (140 ml.) of concentrated hydrochloric acid was added and the mixture refluxed for an additional 5 hr. The aqueous layer was removed, diluted with water and extracted with ether (4 × 100 ml.). The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate solution (100 ml.) and dried ($MgSO_4$). Removal of solvents afforded a residue which on distillation gave impure 2,2-dimethyltetralin (6·9 g., 55%), b. p. 38—44°/0·15—0·45 mm., n_D^{20} 1·5203—1·5243 (lit.,[35] b. p.

[34] Asahina and Momose, *J. Pharm. Soc. Japan*, 1944, **64**, 153.
[35] Clemo and Dickenson, *J.*, 1937, 255.
[36] Sengupta, *J. prakt. Chem.*, 1938, **151**, 82.

104°/12 mm.), and impure 2,2-dimethyl-1-tetralone (1·16 g., 9%), b. p. 48—62°/0·10—0·15 mm., n_D^{20} 1·5328—1·5418.

(iii) **3,3-*Dimethyl*-1-*tetralone*.** The impure 2,2-dimethyltetralin (6·5 g.) was oxidised by chromic–acetic acid. Distillation of the product gave unchanged 2,2-dimethyltetralin (2·6 g., 40%), b. p. 44—48°/0·4—0·45 mm., $n_D^{20\cdot5}$ 1·5190—1·5218, and a mixture of 2,2- and 3-3-dimethyl-1-tetralones (3·0 g., 42%; b. p. 68—80°/0·4—0·85 mm., $n_D^{20\cdot5}$ 1·5312—1·5405). Brady's reagent (from 4·0 g. of 2,4-dinitrophenylhydrazine in 25 ml. of methanol) was added to the mixed tetralones (2·9 g.) in methanol (20 ml.). The orange precipitate, which was formed after 1 min., was removed after 15 min., washed with methanol, and recrystallised from chloroform–ethanol to give pure **3,3-*dimethyl*-1-*tetralone* 2,4-*dinitrophenylhydrazone*** (2·3 g., 39%) as bright-orange needles, m. p. 193—194° (Found: C, 61·0; H, 5·5; N, 15·5. $C_{18}H_{18}N_4O_4$ requires C, 61·0; H, 5·1; N, 15·8%). The ketone was regenerated from this derivative by Demaecker and Martin's method,[37] and redistillation of the crude product gave 3,3-dimethyl-1-tetralone (0·56 g., 64%), b. p. 70—84°/0·2—0·3 mm., n_D^{21} 1·5386—1·5405, which was used without furher purification in the next stage.

(iv) **1,2-*Dihydro*-2,2-*dimethylnaphthalene*.** Reduction of 3,3-dimethyl-1-tetralone (0·50 g.) by potassium borohydride as described for 1,2-dihydro-6-methylnaphthalene gave 1,2-dihydro-2,2-dimethylnaphthalene (0·36 g., 79%).

Synthesis of **1,2-*Dihydro*-6-*methoxy*-1,1-*dimethylnaphthalene*.**—(i) **1-*Bromo*-3-m-*methoxyphenylpropane*.** Reaction of phosphorus tribromide with 3-*m*-methoxyphenylpropan-1-ol [38] (26 g.) by Newman and Wotiz's procedure [39] furnished 1-bromo-3-*m*-methoxyphenylpropane (25 g., 66%), b. p. 85—86°/0·15 mm., n_D^{21} 1·5471 (lit.,[40] b. p. 85—86°/1·1 mm.) (Found: C, 52·4; H, 6·0; Br, 35·3. Calc. for $C_{10}H_{13}BrO$: C, 52·4; H, 5·7; Br, 34·9%).

(ii) **4-m-*Methoxyphenyl*-1,1-*dimethylbutan*-1-*ol*.** " AnalaR " acetone (16·5 ml.) in ether (30 ml.) was added slowly with stirring to a solution of the Grignard reagent from 1-bromo-3-*m*-methoxyphenylpropane (25 g.) in ether (120 ml.) during ½ hr. The stirred mixture was refluxed for a further 5 hr., treated with saturated aqueous ammonium chloride solution (200 ml.), and extracted with ether. Removal of the ether from the dried ($MgSO_4$) extract and distillation of the residue gave a low-boiling substance (5·4 g.), b. p. 38—120°/0·7—0·9 mm., $n_D^{22\cdot5}$ 1·4560—1·4810 and crude **4-*m*-methoxyphenyl-1,1-dimethylbutan-1-ol** (16·1 g., 68%), b. p. 120—127°/0·5—1·0 mm., $n_D^{22\cdot5}$ 1·5117—1·5180.

(iii) **6-*Methoxy*-1,1-*dimethyltetralin*.** Cyclodehydration of 4-*m*-methoxyphenyl-1,1-dimethylbutan-1-ol (5·3 g.) by hydrofluoric acid furnished **6-*methoxy*-1,1-*dimethyltetralin*** (3·8 g., 80%), b. p. 77—81°/0·3 mm., n_D^{21} 1·5324, τ 8·78, 8·36, 7·30, 6·31, 3·54, 3·37, 2·97, 2·80 (Found: C, 82·0; H, 9·5. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

(iv) **1,2-*Dihydro*-6-*methoxy*-1,1-*dimethylnaphthalene*.** Treatment of 6-methoxy-1,1-dimethyltetralin with *N*-bromosuccinimide and dehydrobromination of the product by the methods described in Part XIII [8] gave 1,2-dihydro-6-methoxy-1,1-dimethylnaphthalene.

Synthesis of **1,2-*Dihydro*-7-*methoxy*-1,1-*dimethylnaphthalene*.**—(i) **4-*p*-Methoxyphenyl-1,1-dimethylbutan-1-ol** was prepared in 54% yield from 1-bromo-3-*p*-methoxyphenylpropane [41] as described above for the *m*-isomer and had b. p. 118—122°/0·1 mm., n_D^{21} 1·5138—1·5143.

(ii) **7-*Methoxy*-1,1-*dimethyltetralin*.** Cyclodehydration of the 4-*p*-methoxyphenyl-1,1-dimethylbutan-1-ol (5·3 g.) by hydrofluoric acid furnished **7-*methoxy*-1,1-*dimethyltetralin*** (3·3 g., 68%), b. p. 76—81°/0·1—0·2 mm., n_D^{20} 1·5325 (Found: C, 82·3; H, 9·8%).

(iii) **6-*Methoxy*-4,4-*dimethyl*-1-*tetralone*.** 7-Methoxy-1,1-dimethyltetralin (2·1 g.) was oxidised by chromic–acetic acid to an oil (1·7 g.), n_D^{21} 1·5586, which was converted into **6-*methoxy*-4,4-*dimethyl*-1-*tetralone* 2,4-*dinitrophenylhydrazone*** (1·2 g., 43%), orange-red prisms, m. p. 272° (Found: C, 58·8; H, 5·2; N, 14·2. $C_{19}H_{20}N_4O_5$ requires C, 59·4; H, 5·2; N, 14·6%). This derivative was decomposed by Demaecker and Martin's method [37] to an oil, n_D^{20} 1·5607, which was used without further purification in the next stage.

(iv) **1,2-*Dihydro*-7-*methoxy*-1,1-*dimethylnaphthalene*.** 6-Methoxy-4,4-dimethyl-1-tetralone (0·6 g.) in anhydrous ether (20 ml.) was added to a stirred suspension of lithium aluminium hydride (0·2 g.) in ether (20 ml.) during 10 min. The mixture was worked up in the usual way

[37] Demaecker and Martin, *Nature*, 1954, **173**, 266.
[38] Robinson and Schlittler, *J.*, 1935, 1288.
[39] Newman and Wotiz, *J. Amer. Chem. Soc.*, 1949, **71**, 1292.
[40] Quelet, Raymonde, Durand-Dran, and Pineau, *Compt. rend.*, 1957, **244**, 1218.
[41] Zanden, *Proc. Acad. Sci. Amsterdam*, 1937, **40**, 706.

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TABLE 4.

Principal peaks in the ultraviolet spectra of 1-tetralones.

Subst.	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε
Parent			2480	12,600			2920	1780
2,2-Me_2			2450	9800			2920	940
3,3-Me_2	2120	22,500	2610	6600	2700	5500	3020	2130
6-MeO	2250	12,300	2740	15,100				
6-MeO-1,1-Me_2	2250	14,200	2760	15,400				
6-Me			2550	14,400			2860	2160
6-Cl			2550	16,200			2860	2170
7-MeO	2250	19,350	2520	10,200			3200	2290
7-Me			2500	12,650			3030	1920
7-NHAc	2380	34,500					3200	2030
7-Cl			2450	10,100			3020	1890
7-Br			2450	8350			3020	1465
7-NO_2	2350	21,800	2700	8650				

TABLE 5.

Principal peaks in the ultraviolet spectra of 1,2-dihydronaphthalenes.

Subst.	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε
Parent			2120	25,400			2600	9300				
1,1-Me_2	2110	21,500	2160	22,200	2230	15,800	2590i	10,100	2640	10,200		
2,2-Me_2	2110	29,100	2160	41,000	2230	18,200	2590	10,700	2640	10,800	2960	660
7-MeO			2150	16,800			2700	12,800				
7-MeO-1,1-Me_2			2120	21,200			2700	14,800				
7-Me			2220	15,900			2650	11,500				
7-Cl	2130	16,450	2180	17,300			2650	9700				
6-MeO			2220	28,800			2600	7350			3020	2880
6-MeO-1,1-Me_2			2200	27,500			2610	7500	2700	6000	3020	2450
6-Me			2180	24,200			2620	9070			3020	960
6-NHAc			2410	46,800							3020	1400
6-Cl			2200	28,600			2620	8050				
6-Br			2200	30,900			2620	8150			2930	1340
6-NO_2			2570	31,500							3350	2100

i = inflexion.

TABLE 6.

Principal peaks ($cm.^{-1}$) in the infrared spectra of 1,2-dihydronaphthalenes.

Parent: 1629w, 1600w, 1570w, 1482s, 1035m, 1024m, 1007m, 954w, 937m, 882m, 867w, 804w, 781s 746s, 692s, 682m.

1,1-Me_2: 1642w, 1600w, 1567w, 1479s, 993m, 968w, 938w, 872m, 785s, 754s, 689s, 678w.

2,2-Me_2: 1637w, 1600w, 1570w, 1484m, 972w, 938w, 881w, 805m, 778s, 755w, 736m, 704s.

7-MeO: 1626m, 1608s, 1569s, 1495s, 1250s, 1039s, 1013m, 967w, 943w, 891w, 876m, 849m, 817s, 780w, 754w, 713w, 688m.

7-MeO-1,1-Me_2: 1634w, 1608s, 1563s, 1497s, 1241s, 1046s, 1014w, 993m, 970w, 872m, 853w, 834s, 821m, 811m, 766w, 698m, 679m.

7-Me: 1639w, 1608m, 1563w, 1496m, 1029w, 1014m, 955w, 946w, 891w, 876m, 824s, 783m, 754w, 713w, 689m.

7-Cl: 1631w, 1592m, 1560w, 1479s, 1027w, 1012m, 958w, 935w, 887w, 876m, 842m, 826s, 798w, 779w, 751w, 683m.

6-MeO: 1629w, 1603s, 1571s, 1494s, 1261s, 1041s, 1027m, 1010w, 944w, 876m, 854m, 813m, 779m, 751w, 725w, 695m, 684w.

6-MeO-1,1-Me_2: 1642w, 1605s, 1563s, 1490s, 1252s, 1038s, 995w, 926m, 917w, 871m, 857m, 846w, 818m, 798m, 764m, 702s.

6-Me: 1626w, 1606m, 1569m, 1490s, 1025w, 1009m, 951w, 944w, 877s, 811s, 784s, 750w, 716w, 692s, 676s.

6-NHAc: 1658s, 1614s, 1559s, 1533m, 1495m, 1019w, 1012w, 986w, 887s, 874w, 831m, 792w, 759w, 724m, 696m.

6-Cl: 1627w, 1595s, 1558m, 1482s, 1026m, 1008m, 955w, 935s, 878s, 851s, 813s, 778s, 746m, 702s, 685s.

6-Br: 1629w, 1590m, 1555w, 1476s, 1026w, 1009w, 956w, 934w, 878m, 836s, 810s, 776s, 745w, 698w, 683s.

6-NO_2: 1626w, 1610s, 1585s, 1516s, 1482s, 1341s, 1032w, 1010m, 953w, 937m, 905s, 883w, 861w, 843m, 826s, 805s, 776s, 741s, 702w, 684s.

to give crude 6-methoxy-4,4-dimethyl-1-tetralol (0·6 g., 99%), n_D^{21} 1·547. This was heated to 160° with freshly fused potassium hydrogen sulphate, cooled, and distilled to give 1,2-dihydro-7-methoxy-1,1-dimethylnaphthalene.

Ultraviolet-light absorption data for the 1-tetralones and 1,2-dihydronaphthalenes are recorded in Tables 4 and 5. Infrared absorption data for 1,2-dihydronaphthalenes are given in Table 6.

Physical constants and analytical data of the 1,2-*dihydronaphthalenes*, prepared as indicated above, are listed in Table 7.

Preparative Dehydrogenations.—General method. A solution of the dihydronaphthalene and tetrachloro-1,2-benzoquinone in benzene was refluxed under pure, dry nitrogen for several hours. The resulting solution was passed down an alumina column (to remove quinol and any unchanged quinone), and eluted with benzene. Removal of the benzene from the eluate afforded material which was examined as indicated below for the presence of the appropriate naphthalene.

(a) 1,2-*Dihydro*-7-*methoxynaphthalene*. The dihydronaphthalene (39 mg.), the quinone (60 mg.), and benzene (10 ml.) were refluxed for 2 hr. The evaporated eluate (38 mg., 99%) had m. p. 63—69°: (2-methoxynaphthalene [42] has m. p. 72°).

(b) 1,2-*Dihydro*-6-*methoxynaphthalene*. The dihydronaphthalene (0·76 g.), the quinone (1·15 g.), and benzene (10 ml.) were refluxed for 2 hr. The evaporated eluate (0·76 g., 100%) had m. p. and mixed m. p. 70—72°, $\lambda_{max.}$ 2260 (ε 75,000), 2610 (ε 3550), 2710 (ε 4820), 2820 (ε 3320), 3130 (ε 1580), 3200 (ε 1360), 3280 Å (ε 2120). 2-Methoxynaphthalene [43] had m. p. 71·5—72·5°, and $\lambda_{max.}$ 2260 (ε 72,700), 2610 (ε 4270), 2710 (ε 4740), 2820 (ε 3320), 3130 (ε 1550), 3200 (ε 1330), 3270 Å (ε 2130).

TABLE 7.

Substituted 1,2-dihydronaphthalenes.

				Found (%)				Required (%)		
Subst.	Yield (%)	B. p./mm.	n_D^t	C	H	Hal or N	Formula	C	H	Hal or N
None *	—	40°/0·8	1·5822$^{21.5}$	92·1	7·9	—	$C_{10}H_{10}$	92·3	7·7	—
7-MeO * ...	26 [a]	105—107°/3·5	1·5852^{21}	82·2	7·7	—	$C_{11}H_{12}O$	82·5	7·6	—
6-MeO	64 [a]	82°/1·3	1·5777^{27}	82·6	7·6	—	$C_{11}H_{12}O$	82·5	7·6	—
7-Me	43 [a]	68°/1·7	1·5735^{22}	91·5	8·7	—	$C_{11}H_{12}$	91·6	8·4	—
6-Me *	71 [a]	103—107°/14	1·5725$^{21.5}$	91·9	8·7	—	$C_{11}H_{12}$	91·6	8·4	—
6-NHAc ...	100 [a, c]	m. p. 70—71°	—	77·0	7·1	7·4	$C_{12}H_{13}NO$	77·0	7·0	7·5
7-Cl	53 [a]	78°/1·3—1·4	1·5928^{26}	72·7	5·6	20·6	$C_{10}H_9Cl$	73·0	5·5	21·5
6-Cl	66 [a]	67°/0·1	1·5941^{21}	72·9	5·8	21·6	$C_{10}H_9Cl$	73·0	5·5	21·5
6-Br	77 [a]	89—90°/1	1·6185^{21}	57·2	4·4	38·1	$C_{10}H_9Br$	57·4	4·3	38·2
6-NO_2	66 [a]	120—124°/1	1·6166^{24}	68·3	5·2	8·2	$C_{10}H_9NO_2$	68·6	5·2	8·0
1,1-Me_2 * ...	51 [b]	53—56°/0·6—0·7	1·5570^{16}	90·9	9·0	—	$C_{12}H_{14}$	91·1	8·9	—
2,2-Me_2 ...	79 [a]	40—44°/0·4	1·5451^{22}	91·3	9·1	—	$C_{12}H_{14}$	91·1	8·9	—
7-MeO-1,1-Me_2	49 [a]	70—82°/0·3	1·5615^{21}	83·1	8·6	—	$C_{13}H_{16}O$	82·9	8·6	—
6-MeO-1,1-Me_2	27 [b]	73—75°/0·15	1·5579^{23}	83·2	8·7	—	$C_{12}H_{16}O$	82·9	8·6	—

* Known compounds. [a] From ketone. [b] From tetralin. [c] Crude.

(c) 1,2-*Dihydro*-7-*methylnaphthalene*. The hydrocarbon (42 mg.), the quinone (71 mg.), and benzene (10 ml.) were refluxed for 2 hr. The evaporated eluate (35 mg., 83%) had an infrared spectrum identical with that of 2-methylnaphthalene (British Drug Houses Ltd.), m. p. 34—35° (lit.,[44] m. p. 34°).

(d) 1,2-*Dihydro*-6-*methylnaphthalene*. The hydrocarbon (0·69 g.), the quinone (1·16 g.), and benzene (10 ml.) were refluxed for 2 hr., then diluted with light petroleum (b. p. 40—60°), kept at room temperature for 1 hr., and filtered. The precipitate (0·4 g., 34%), m. p. 190—193°, sublimed to give pure tetrachlorocatechol, m. p. 193°, mixed m. p. 190—192° (lit.,[22] m. p. 193°). Chromatography of the filtrate afforded 2-methylnaphthalene (0·55 g., 81%), m. p. 33° and mixed m. p. 33—35°, $\lambda_{max.}$ 2230 (ε 58,300), 2660 (ε 4120), 2760 (ε 4550), 2860 (ε 3120), 3050

[42] Staedel, *Annalen*, 1883, **217**, 40.
[43] Hiers and Hager, *Org. Synth.*, Coll. Vol. I (2nd edn.), p. 58.
[44] Mair and Streiff, *J. Res. Nat. Bur. Stand.*, 1940, **24**, 395.

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(ε 570), 3130 (ε 360), 3190 Å (ε 570); the pure hydrocarbon had $\lambda_{max.}$ 2230 (ε 67,500), 2650 (ε 4260), 2750 (ε 4690), 2860 (ε 3270), 3050 (ε 570), 3120 (ε 369), 3180 Å (ε 611).

(e) 6-*Acetamido*-1,2-*dihydronaphthalene*. The dihydronaphthalene (190 mg.), the quinone (250 mg.), and benzene (10 ml.) were refluxed for 52 hr. A purple precipitate (3 mg.) was removed and the filtrate chromatographed in the usual manner except that 5% ethanol in benzene was used as eluant. The evaporated eluate (220 mg., 100%) had m. p. 128—130°, $\lambda_{max.}$ 2420 (ε 47,300), 2490 (ε 42,200), 2730 (ε 6660), 2830 (ε 7680), 2940 (ε 7030), 3150 (ε 850), 3300 Å (ε 850) (2-acetamidonaphthalene [45] has m. p. 132°). 2-Acetamidonaphthalene, prepared by acetylation of 2-naphthylamine, m. p. 132—134°, had $\lambda_{max.}$ 2430 (ε 57,000), 2500 (ε 48,000), 2740 (ε 7700) 2840 (ε 8950), 2950 (ε 6450), 3160 (ε 1000), 3320 Å (ε 980).

(f) 7-*Chloro*-1,2-*dihydronaphthalene*. The dihydronaphthalene (48 mg.), the quinone (72 mg.), and 1,2-dichlorobenzene were heated to 90° for 4 hr. The evaporated eluate (25 mg., 52%) had an infrared spectrum which included naphthalenoid peaks.

(g) 6-*Chloro*-1,2-*dihydronaphthalene*. The dihydronaphthalene (184 mg.), the quinone (300 mg.), and benzene (3 ml.) were refluxed for 3 hr. The evaporated eluate (162 mg., 89%) had m. p. 56—57°, $\lambda_{max.}$ 2255 (ε 48,700), 2670 (ε 5030), 2700 (ε 4710), 2770 (ε 5360), 2880 (ε 3570), 3070 (ε 400), 3220 Å (ε 430). 2-Chloronaphthalene [46] has m. p. 56—57°, $\lambda_{max.}$ 2630 (ε 5700), 2700 (ε 5400), 2760 Å (ε 6300).

(h) 6-*Bromo*-1,2-*dihydronaphthalene*. The dihydronaphthalene (500 mg.), the quinone (590 mg.), and benzene (5 ml.) were refluxed for 3 hr. The evaporated eluate (430 mg., 87%) had m. p. 52—54°, $\lambda_{max.}$ 2270 (ε 63,600), 2680 (ε 4540), 2710 (ε 4440), 2780 (ε 4850), 2890 (ε 4050), 3070 (ε 350), 3130 (ε 220), 3220 (ε 260). 2-Bromonaphthalene [47] has m. p. 55—56°. 2-Bromonaphthalene (British Drug Houses Ltd.), m. p. 55°, had $\lambda_{max.}$ 2260 (ε 80,000), 2680 (ε 5000), 2710 (ε 4800), 2780 (ε 5460), 2890 (ε 3630), 3070 (ε 404), 3220 Å (ε 300).

(i) 1,2-*Dihydro*-6-*nitronaphthalene*. The dihydronaphthalene (690 mg.), the quinone (970 mg.), and benzene (10 ml.) were refluxed for 19 hr. The evaporated eluate (670 mg., 99%) had m. p. 70°, $\lambda_{max.}$ 2540 (ε 23,200), 2610 (ε 23,700), 3030 Å (ε 7790) (2-nitronaphthalene [48] has m. p. 79°). Recrystallisation from ethanol gave pure 2-nitronaphthalene, m. p. 77°, $\lambda_{max.}$ 2540 (ε 23,300), 2610 (ε 24,400), 3030 Å (ε 9990).

(j) 1,2-*Dihydro*-2,2-*dimethylnaphthalene*. The hydrocarbon (44 mg.), the quinone (70 mg.), and benzene (2 ml.) were refluxed for 4 hr. The evaporated eluate (21 mg., 48%) had $\lambda_{max.}$ 2170 Å (ε 24,200), $\lambda_{infl.}$ 2270 (ε 18,800), 2550 (ε 2590), 2830 (ε 1380), $\lambda_{max.}$ 2910 (ε 1260), $\lambda_{infl.}$ 3010 (ε 1080), 3070 (ε 820) $\lambda_{max.}$ 3210 Å (ε 156).

(k) 1,2-*Dihydro*-7-*methoxy*-1,1-*dimethylnaphthalene*. The dihydronaphthalene (87 mg.), the quinone (115 mg.), and benzene (3 ml.) were refluxed for 1 hr. The evaporated eluate (82 mg., 95%), n_D^{20} 1·606, had $\lambda_{max.}$ 2330 (ε 17,300), 2800 (ε 2600), $\lambda_{infl.}$ 3150 (ε 705), $\lambda_{max.}$ 3300 Å (ε 630).

(l) 1,2-*Dihydro*-6-*methoxy*-1,1-*dimethylnaphthalene*. The dihydronaphthalene (92 mg.), the quinone (120 mg.), and benzene (2 ml.) were refluxed for 2 hr. The evaporated eluate (43 mg., 47%) had $\lambda_{max.}$ 2270 (ε 55,700), 2560 (ε 4650), 2650 (ε 5390), 2750 (ε 5020), 2870 (ε 3720), 3070 (ε 1880), 3150 (ε 2120), 3220 (ε 2320), 3300 (ε 2120), 3360 Å (ε 2690).

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[45] Liebermann, *Annalen*, 1876, **183**, 225.
[46] Ferguson, *J.*, 1954, 304.
[47] Newman and Wise, *J. Amer. Chem. Soc.*, 1941, **63**, 2847.
[48] Fierz-David and Sponagel, *Helv. Chim. Acta*, 1943, **26**, 98.

946. *Cyclisations and Rearrangements in the Isodrin–Aldrin Series.*

By C. W. Bird, R. C. Cookson, and E. Crundwell.

Treatment of the stereoisomeric insecticides, isodrin and aldrin, with acid induces a series of cyclisation, rearrangement, and hydride transfer to form a mixture of saturated and unsaturated products, the most stable of which is the saturated isomer with a cyclobutane ring in place of the two double bonds of isodrin. On reaction with acid and on acetolysis of the methanesulphonates of related alcohols five different ring systems are produced.

The results, *inter alia*, prove the configurations previously assumed for isodrin and aldrin, whose ring systems have now been interconverted.

The isomeric chlorohydrocarbon insecticides, aldrin and isodrin, offer attractive frameworks for the study of transannular interactions, both chemical and spectroscopic: but first their configurations must be considered.

Aldrin is made [1] by the addition of bicycloheptadiene to hexachlorocyclopentadiene: knowing the tendency for *exo*-addition of dienes to bicycloheptadiene [2] and allowing for the large size of the *gem*-dichloro-group, one might expect aldrin to have the configuration (I) rather than any of the other three possibilities. Isodrin is made [3] by addition of hexachlorobicycloheptadiene (II) to cyclopentadiene: here the large *gem*-dichloro-group in the dienophile (II) is likely to force addition of cyclopentadiene from the *endo*-side. Of the two structures resulting from *endo*-addition, (III) avoids the repulsion between the methylene and dichloroethylene groups present in the other.

The double bonds in a diene of structure (III) are very close to one another and on irradiation would be expected to join up forming a cyclobutane ring.[4] We therefore applied the test of irradiating a solution of isodrin in a silica vessel with a mercury arc. That the product was saturated was shown by the usual chemical tests, and the disappearance of the dichloroethylene chromophore was confirmed by the absence of its characteristic, strong band at about 1600 cm.$^{-1}$. The low end-absorption of the product at 200 mμ, where the dichloroethylene compounds have ε about 9000, definitely established that the product was saturated. Since systematic names in this series are so cumbersome * we shall refer to this isomer as the cage-compound (IV). Its formation by treatment that left aldrin unchanged proves the configuration of isodrin (III). The isodrin and aldrin series are interconvertible by rearrangements that affect only the unchlorinated part of the molecule (see below): aldrin must, therefore, have the configuration (I).

Attention was next turned to the action of electrophilic reagents on isodrin (III), as its stereochemistry clearly favours transannular reactions. Indeed the products obtained on treatment of isodrin with sulphuric acid in wet dioxan were entirely saturated. The two main components were the cage-compound (IV) and an alcohol, m. p. 204°. We learnt later that Lidov and Bluestone had described in a patent [5] the conversion of isodrin

* In a preliminary note (Cookson and Crundwell, *Chem. and Ind.*, 1958, 1004) we wrote that we were tempted to call this isomer " photodrin: " the Editors have since persuaded us to resist the temptation. The following descriptive names are used in this paper: isodrin (III), cage-compound (IV), *endo-endo*-alcohol (V; R = H), aldrin (I), *endo-exo*-alcohol (IX; R = H), half-cage *exo*-alcohol (VI; H = R), half-cage *endo*-alcohol (XII; R = H). Systematic names are given in the Experimental section. We are most grateful to the Editors for their assistance in naming these molecules on the " polycyclo " convention, to which α- and β-prefixes have been added to distinguish stereoisomers (see footnote, p. 4814.)

[1] Lidov, U.S.P. 2,635,977; Lidov and Soloway, B.P. 692,547.

[2] Alder, Mönch, and Wirtz, *Annalen*, 1959, **627**, 47; Stille and Frey, *J. Amer. Chem. Soc.*, 1959, **81**, 4273.

[3] Bluestone, U.S.P. 2,676,132; Lidov, U.S.P. 2,717,851; Arvey Corp., B.P. 714,688.

[4] Cookson, Crundwell, and Hudec, *Chem. and Ind.*, 1958, 1003; Schönberg, " Präparative Organische Photochemie," Springer-Verlag, Berlin, 1958, p. 22.

[5] Lidov and Bluestone, U.S.P. 2,714,617.

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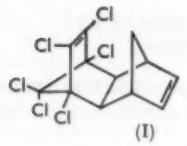
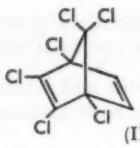
into a substance clearly the same as (IV) by hydrogen bromide in ether or acetic acid. Lidov [3] had added acetic acid to isodrin (III) in the presence of sulphuric acid to form an acetate, which he assumed had the unrearranged structure (V). Hydrolysis of the acetate yielded the alcohol, m. p. 204°, which could be re-acetylated to Lidov's acetate. The absence of the dichloroethylene chromophore and their complete saturation rule out structures (V) for the alcohol and its acetate. The ketone got by oxidation of the alcohol had $\nu_{max.}$ 1755 cm.$^{-1}$ and no band at 1420 cm.$^{-1}$, so that the carbonyl group must be in a five-membered ring with no α-methylene group. These features are accommodated by structure (VI; R = H) for the alcohol, m. p. 204°, and (VII) for the ketone. Boron trifluoride in benzene rearranged isodrin epoxide (VIII) quantitatively to the ketone (VII).†


(I)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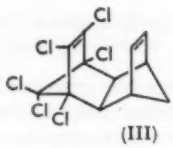
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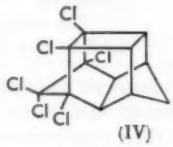
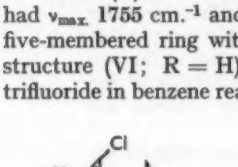

(IV)

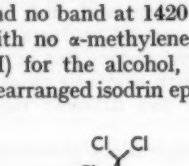
(V)

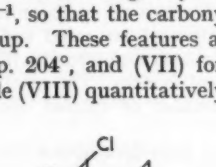
(VI)

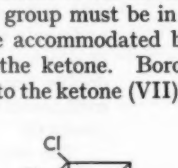
(VII)

(VIII)


(IX)


(X)


(XI)


(XII)

The genuine, unrearranged hydroxydihydro-derivative (V; R = H), still showing the dichloroethylene chromophore, was made from isodrin by Brown and Zweifel's reaction.[6]

Acetic acid containing sulphuric acid turned aldrin (I) almost entirely into the *endo-exo*-acetate (IX; R = Ac), accompanied by traces of half-cage acetate (VI; R = Ac) and cage-compound (IV). From its mechanism of formation the acetate (IX) was expected to be the *exo*-epimer, and this configuration was confirmed by the compound's being different from the known [7] *endo*-epimer, made by addition of *endo*-acetoxybicycloheptene to hexachlorocyclopentadiene.

To examine the kinetically controlled, consecutive rearrangements of the intermediate carbonium ions, the methanesulphonates of the *endo-endo*-alcohol (V), half-cage alcohol (VI), and *endo-exo*-alcohol (IX) were heated in acetic acid containing sodium acetate. The last (IX) gave mostly aldrin (I) with some *endo-exo*-acetate (IX; R = Ac) and *endo-endo*-acetate (V; R = Ac), but major products from the other two methanesulphonates, which were acetolysed far more rapidly, were a new acetate and a chlorohydrocarbon. The dichloroethylene chromophore was absent from the spectra of both, so that we assumed at first that they were the acetate (XI; R = Ac) and the olefin (X) formed by further rearrangement of a carbonium ion related to the half-cage structure (VI). On

† In the ultraviolet region the three isomeric ketones, *endo-endo*-ketone (as V), half-cage ketone (VII; X = O), and *endo-exo*-ketone (as IX) all had very similar long-wavelength absorption, with $\lambda_{max.}$ between 295 and 300 mμ and $\varepsilon_{max.}$ 30—60, so that the dichloroethylene group has little effect on the $n \longrightarrow \pi^*$ transition of the first ketone (as V).

[6] Brown and Zweifel, *J. Amer. Chem. Soc.*, 1959, **81**, 247.

[7] Lidov, U.S.P. 2,635,979; Lidov and Soloway, B.P. 692,545; Vol'fson, Mel'nikov, Plate, Sapozhkov, and Taits, *Doklady Akad. Nauk S.S.S.R.*, 1955, **105**, 1252.

TABLE 1. *Solvolysis products of methanesulphonates in acetic acid–sodium acetate.*

Methanesulphonate	Isodrin (III)	*endo-endo*-Acetate (V)	*exo*-Half-cage acetate (VI)	Cage compound (IV)	Chlorohydrocarbon (XIII)	Half-cage *endo*-acetate (XII)	Aldrin (I)	*endo-exo*-Acetate (IX)
endo-endo- (V)	38	7·4	8	—	21	25	—	—
exo-Half-cage (VI)	—	—	14	—	34	52	—	—
endo-Half-cage (XII)	—	—	16	—	40	44	—	—
endo-exo- (IX)	—	10	—	—	—	—	75	15

that assumption we supplied samples and experimental details to Professor S. Winstein and Dr. P. Carter, who were also interested in relating the supposed structures to their unchlorinated analogues.[8,9] Surprisingly, on reduction with lithium and t-butyl alcohol in tetrahydrofuran the alcohol derived from the new acetate gave the cyclic ether with the half-cage skeleton, presumably derived from the *endo*-half-cage alcohol (XII; R = H). In agreement with the revised structure (XII: R = Ac), the infrared spectrum of the acetate shows a sharp band at 3140 cm.$^{-1}$ and that of the alcohol one at 3100 cm.$^{-1}$. These exceptionally high frequencies can be attributed only to the C–H stretching mode of a severely congested hydrogen atom:[10] in fact, the methanesulphonate (XII; R = Me·SO_2) has the highest frequency recorded for a hydrogen atom linked to saturated carbon (3145 cm.$^{-1}$). The structure of the alcohol (XII; R = H) was made secure by its oxidation to the same half-cage ketone (VII) as was obtained from its epimer (VI; R = H).

The new chlorohydrocarbon, isomeric with isodrin and aldrin, was found to be saturated, and its precise structure is not yet known. Acid converts it into the cage-compound (IV), so that it may have a structure such as (XIII) (in Scheme 1).

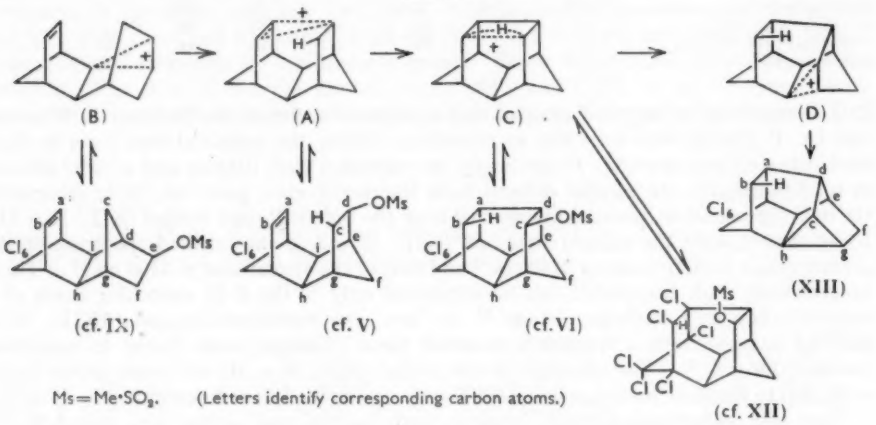
The methanesulphonates were then all solvolysed under identical conditions (18 hr. in boiling acetic acid containing 5% of sodium acetate), and the products were analysed by careful chromatography on silica gel. Separation of the eight possible components was usually good: occasional small intermediate fractions were analysed by infrared spectroscopy. [Rather surprisingly the cage-compound (IV) travelled more slowly down the column than isodrin.] Table 1 records the molar percentage yields of the products from these solvolyses: the figures for the *endo-exo*-methanesulphonate (IX: R = Me·SO_2) refer to 190°, since it was quite stable under the standard conditions.

The ionisation of the other three sulphonates must be accelerated very substantially, either through relief of strain or delocalisation of charge in the transition state. The obvious factor in the *endo-endo*-ester (V; R = Me·SO_2) is the ability of the electrons of the double bond to participate,[8] so that the first carbonium ion it forms is (A), in Scheme 1. In any case, the quite different distribution of products (unlikely to be entirely due to the difference in temperature) shows that it does not give the same ion (B) as the *endo-exo*-methanesulphonate (IX; R = Me·SO_2). Release of pressure between the hydrogen atoms attached to $C_{(b)}$ and $C_{(c)}$ must contribute to the accelerated solvolysis of the half-cage *exo*-sulphonate (VI; R = Me·SO_2). Further help may come from involvement of electrons from the $C_{(b)}$–H bond [to give the ion (C)], from the $C_{(a)}$–$C_{(d)}$ bond, or from the $C_{(g)}$–$C_{(h)}$ bond [to give ion (D)]. For the sake of illustration, the first alternative is implied in the diagram. Ionisation of the half-cage *endo*-sulphonate (XII; R = Me·SO_2), which must receive even more steric acceleration, may proceed initially to an ion-pair such as (H; R = Me·SO_2). The chlorohydrocarbon (XIII) is supposed to be formed by loss of a proton from the bornyl type of bridged ion (D). In the presence of acid the rearrangements become reversible: a proton adds to the $C_{(b)}$–$C_{(g)}$ bond of the cyclopropane (XIII) to regenerate the ion (D), which eventually loses a proton, perhaps *via* (C), to give the

[8] Winstein, *Experientia*, Suppl. II, 1955, 137.
[9] Bruck, Winstein, and Thompson, *Chem. and Ind.*, 1960, 590.
[10] de Vriess and Ryason, *J. Org. Chem.*, 1961, **26**, 62; Kivelson, Winstein, Bruck, and Hansen, *J. Amer. Chem. Soc.*, in the press.

cage-compound (IV). [If an ion like (C) exists it must be unsymmetrical in this system, the proton being nearer $C_{(b)}$ than to $C_{(e)}$. We hope to find which proton is actually lost in the cyclisation of (V), (VI), and (XII) to the cage-compound (IV) by using deuterated compounds.]

Scheme 1.



Ms = Me·SO_2. (Letters identify corresponding carbon atoms.)

The most extraordinary feature of these rearrangements, however, is that the very strained half-cage *endo*-acetate (XII; R = Ac) is formed from the sulphonates (V), (VI), and (XII) (R = Me·SO_2) about three times as fast as is the *exo*-acetate (VI; R = Ac). All the obvious ways of delocalising the positive charge in the half-cage carbonium ion operate from the inside (*endo*), and even apart from steric hindrance would lead to the confident expectation of *exo*-attack by acetate ion. Perhaps the relatively acidic hydrogen atom attached to $C_{(b)}$ can help to pull the acetate into the inside of the molecule by hydrogen-bonding in a transition state resembling (H; R = Ac).

Although the differences in ratios of half-cage *exo*-acetate (VI; R = Ac) to *endo*-acetate (XII; R = Ac) to the chlorohydrocarbon (XIII?) seem outside the experimental error, the ratios are nevertheless rather close in all three acetolyses, so that these three products may all arise from a common ion (D). In acetolysis the hydride migration is irreversible, and no trace of product with the isodrin or aldrin skeleton could be found from the half-cage methanesulphonates. Although the cage-compound (IV) was never detected from acetolysis of the methanesulphonates, preliminary experiments show that it is formed on treatment of the half-cage amine with nitrous acid. The *endo-exo*-sulphonate (IX; R = Me·SO_2) gave some *endo-endo*-acetate (V; R = Ac), presumably through the ion (A). It is remarkable, then, that no isodrin or rearranged products could be isolated, which seem to be derived from the ion (A) in acetolysis of the *endo-endo*-methanesulphonate (V; R = Me·SO_2). Although the difference in temperature may be partly responsible, this may mean that different ions are involved.

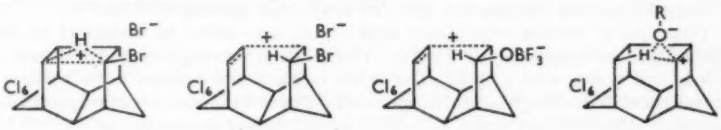
Table 2 shows the result of heating compounds of the four ring systems with 5% sulphuric acid in acetic acid for ½ hr. Under these conditions of equilibration the isodrin skeleton (III and V; R = Ac) soon disappears; the aldrin skeleton (IX; R = Ac) is relatively stable, but gradually goes over to the half-cage *exo*-acetate (VI; R = Ac) and the cage-compound (IV); the *endo*-acetate (XII; R = Ac) and chlorohydrocarbon (XIII?) soon rearrange to the same two systems; and the half-cage *exo*-acetate (VI: R = Ac) itself slowly cyclises to the cage-compound, the most stable system, which eventually constitutes almost the sole product.

From the addition of acetic acid to isodrin (III) the half-cage acetate (VI; = Ac) R

TABLE 2. *Products of heating with* H_2SO_4–AcOH.

	Half-cage *exo*-acetate (VI)	Cage compound (IV)	Half-cage *endo*-acetate (XII)	*endo-exo*-Acetate (IX)
Isodrin (III)	57	37	4·5	2
Half-cage *exo*-acetate (VI)	73	27	—	—
Product of acetolysis of half-cage mesylate	53	45	1·8	—
Aldrin (I)	1·8	1·5	—	97

should contain both the added hydrogen and the acetate on the same carbon atom. Addition of deutero-acid gave a sample of acetate (VI; R = Ac) containing deuterium, which was lost on oxidation to the ketone (VII).



(E) (F) (G) (H)

Bromine in carbon tetrachloride transformed isodrin (III) mainly into the cage-compound (IV). Hydrogen bromide was also produced, which might have catalysed the cyclisation, but that the cage-compound was still formed in the presence of a suspension of finely divided calcium carbonate, when no free hydrogen bromide could be detected, shows that bromine does catalyse the cyclisation. Presumably the cage-compound comes from some such ion-pair as (E) or (F) by removal of Br^+ in preference to H^+ by Br^-. It amounts to an electrophilic displacement *with inversion* on $C_{(c)}$.

In contrast, the corresponding dipolar ions (*e.g.*, G) from isodrin oxide (VIII) and boron trifluoride, being unable to lose oxygen by reduction, preferentially undergo hydride migration to give the stable carbonyl group, rather than to lose the inside proton to give the cage-alcohol.

There are several differences in the behaviour of the compounds in the isodrin–aldrin series and of their unchlorinated analogues, on which Winstein and his colleagues [8,9] have published some preliminary results: the most obvious are (1) the much reduced reactivity of the chlorinated double bond (a,b), and (2) the necessity for hydride transfer to $C_{(b)}$ to accompany bridging to $C_{(a)}$ in the chlorinated compounds.

(1) The relative reluctance of the chlorinated double bond to participate in carbonium ion reactions is shown, for example, by the far slower solvolysis of the chlorinated sulphonate (V; R = Me·SO_2) than of the unchlorinated analogue, which cannot even be isolated.[9] Although the cage-compound (IV) is not formed in our acetolyses, the cage-hydrocarbon is an important product in the chlorine-free series.[8,9]

(2) The reluctance of the carbon atoms carrying chlorine to accept a positive charge or a nucleophile means that the half-cage and the skew skeleton can be formed only after hydride migration. In the unchlorinated series the occurrence of hydride migration cannot be detected, because of the symmetry of the system: the use of optically active or isotopically labelled esters would be needed.

[Added 13th March, 1961.] Since this paper was submitted, one has appeared by Soloway, Damiana, Sims, Bluestone and Lidov (*J. Amer. Chem. Soc.*, 1960, 82, 5377), in which they accept structures (VI) and (VII).

EXPERIMENTAL

Infrared spectra were recorded for Nujol or Fluorlube mulls, unless otherwise stated, on a Unicam S.P. 100 spectrophotometer. Ultraviolet spectra were measured for ethanol solutions on a Unicam S.P. 500 or S.P. 700 instrument. Solutions for chromatography were prepared in light petroleum (b. p. 60—80°) and chromatographed on silica gel (activity about 1 on Brockmann's scale) with light petroleum containing increasing proportions of benzene. Compounds were eluted in the following order: (III), (XIII?), (V; R = Ac), (XII; R = Ac), (VI;

R = Ac), and (IV), (I), (V; R = Ac), (IX; R = Ac), (XII; R = Ac), (VI; R = Ac). Where compounds were obtained by alternative routes their identity was established by mixed m. p. and infrared spectra.

Photoisomerisation of Isodrin.—1α,2β,3α-1,8,9,10,11,11-Hexachlorotetracyclo[6,2,1,$1^{3,6}$,$0^{2,7}$]dodeca-4,9-diene * (isodrin) (III) (1 g.) dissolved in ethyl acetate (50 ml.) was irradiated for 7 days in a quartz tube, in an atmosphere of carbon dioxide. The solvent was evaporated, and the residue dissolved in acetone (20 ml.) and treated with potassium permanganate (1·6 g.) in acetone (20 ml.) under reflux for 30 min. Water and sodium metabisulphite were added and the product was isolated by chloroform extraction. The 1,2,3,3,4,11-*hexachlorohexacyclo*-[5,4,1,0,^{2,6},$0^{4,11}$,$0^{5,9}$,$0^{10,12}$]*dodecane* (cage compound; IV) thus obtained crystallised from ethanol in needles, m. p. 298° (decomp.) (Found: C, 39·6; H, 2·3; Cl, 57·8. $C_{12}H_6Cl_6$ requires C, 39·5; H, 2·2; Cl, 58·3%); ε at 200 mμ was 630; no maximum around 1600 cm.$^{-1}$.

Acid Treatment of Isodrin.—Sulphuric acid (5 ml.) was added to isodrin (2 g.) dissolved in dioxan (20 ml.) containing water (0·2 ml.). The solution was kept on a steam-bath for 14 hr., then cooled, and water was added. The ether extract was washed with sodium hydrogen carbonate solution, dried (Na_2SO_4) and evaporated. The residue was chromatographed to give the cage-compound (IV) (0·28 g.) and 1,9,10,10,11,exo-12-*hexachloropentacyclo*[7,2,1,$0^{3,6}$,$0^{4,8}$,$0^{7,11}$]-*dodecan*-3α-*ol* (half-cage alcohol; VI; R = H) (0·62 g.) which crystallised from aqueous ethanol in needles, m. p. 204° (Found: C, 38·1; H, 2·5; Cl, 55·5. $C_{12}H_{10}Cl_6O$ requires C, 37·6; H, 2·6; Cl, 55·5%), no maximum around 1600 cm.$^{-1}$. The half-cage alcohol was acetylated with acetic anhydride in pyridine to give the *acetate* (VI; R = Ac), needles (from ethanol), m. p. 218° (Found: C, 39·9; H, 2·1; Cl, 49·5; Ac, 11·1. $C_{14}H_{12}Cl_6O_2$ requires C, 39·5; H, 2·8; Cl, 50·2; Ac, 10·1%), $\nu_{max.}$ 1740 cm.$^{-1}$; no band around 1600 cm.$^{-1}$. The acetate was reconverted into the alcohol by basic hydrolysis.

Oxidation of the Half-cage Alcohol (VI).—The alcohol (1·25 g.), dissolved in acetic acid (40 ml.), was treated at 70° dropwise, during 40 min., with aqueous potassium permanganate (0·82 g. in 40 ml.). The temperature was raised to 110° and then kept at 90° for 3 hr. The mixture was cooled and filtered. The organic material, separated from the precipitate by extraction with acetone, was chromatographed to give 1α,9,10,10,11,exo-12-*hexachloropentacyclo*-[7,2,1,$0^{3,6}$,$0^{4,8}$,$0^{7,11}$]*dodecan*-3-*one* (VII) (0·82 g.) that, crystallised from benzene–light petroleum, had m. p. 285° (decomp.) (Found: C, 38·1; H, 2·3; Cl, 55·8. $C_{12}H_6Cl_6O$ requires C, 37·8; H, 2·1; Cl, 55·8%), $\lambda_{max.}$ 300 mμ (ε 35); ε at 205 mμ = 480; $\nu_{max.}$ 1755 cm.$^{-1}$; no band around 1600 or 1400 cm.$^{-1}$.

Rearrangement of Isodrin Epoxide.—The epoxide (VIII) (1·26 g.) was dissolved in dry benzene (20 ml.) and saturated with boron trifluoride. The solution was refluxed on the steam-bath for 30 min. and then evaporated to dryness. The residue was chromatographed to give the half-cage ketone (VII) as the sole product.

The endo-endo-*Alcohol* (V; R = H).—Diborane, prepared from sodium borohydride (1·2 g). and boron trifluoride–ether complex (6·4 g.),[11] was passed into an ice-cooled solution of isodrin (11 g.) in dry ether (50 ml.) during 70 min. and the mixture was left at room temperature for 70 min. Ice was then added, followed by sodium hydroxide (0·5 g.) in water (4 ml.). Subsequently a 30% solution (3·75 ml.) of hydrogen peroxide was added during an hour with stirring, which was continued for a further 40 min. The resultant emulsion was washed with ether and the extract washed with 4N-sulphuric acid and water. Evaporation of the ether gave a white, frothy solid (11 g.) which did not crystallise. The product was characterised by acetylation with acetic anhydride in pyridine to 1α,2β,3α,1,8,9,10,11,11-*hexachlorotetracyclo*[6,2,1,$1^{3,6}$,$0^{2,7}$]-*dodec*-9-*en*-4β-*yl acetate* (V; R = Ac); crystallised from ethanol, this had 194—195° (Found: Cl, 49·9; Ac, 9·3. $C_{14}H_{12}Cl_6O_2$ requires Cl, 50·2; Ac, 10·1%), $\nu_{max.}$ 1725, 1600 cm.$^{-1}$.

* The symbols α and β in this and similar names are used to distinguish stereoisomers that would otherwise have identical polycyclo-names. They denote the relative stereochemistry of hydrogen or a substituent at the positions enumerated; the largest ring (*i.e.*, that stated first in the square brackets) is considered to be flat; hydrogen or the substituent at position 1 (which must necessarily be a bridge-head) is arbitrarily assigned an α-prefix; hydrogen and the substituents at other positions are then given α- or β-prefixes according to whether they are on the same or different sides of the " plane " of the large ring. Cage and half-cage structures, at least in this series, can exist in only one configuration and no such stereochemical designation is necessary for these parent structures. It is not necessary to consider here the extension of this system needed for asymmetry on a bridge (here a methylene group of the five-membered rings).

[11] Brown and Rao, *J. Org. Chem.*, 1957, **22**, 1135.

1α,2β,3α,1,8,9,10,11,11-*Hexachlorotetracyclo*[6,2,1,$1^{3,6}$,$0^{2,7}$]*dodec*-9-*en*-4-*one* was prepared by oxidation of the *endo-endo*-alcohol (V; R = H) with chromium trioxide in pyridine [12] and, crystallised from ethanol, had m. p. 220° (Found: C, 38·1; H, 2·4; Cl, 56·0. $C_{12}H_6Cl_6O$ requires C, 37·8; H, 2·1; Cl, 55·8%), $\lambda_{max.}$ 298 mμ (ε 30), $\nu_{max.}$ 1750, 1600, 1425 cm.$^{-1}$.

Preparation of Methanesulphonates.—The appropriate alcohol was dissolved in pyridine, treated with a slight excess of methanesulphonyl chloride, and set aside overnight. Water was cautiously added and the crystals that separated were filtered off and recrystallised. In this way were prepared:

The half-cage exo-*methanesulphonate* (VI; R = SO_2Me), rods (from chloroform), m. p. 201° (decomp.) (Found: C, 33·9; H, 2·9; S, 6·8. $C_{13}H_{12}Cl_6O_3S$ requires C, 33·8; H, 2·6; S, 6·9%).

The endo-endo-*methanesulphonate* (V; R = SO_2Me), flakes (from ethanol), m. p. 135—137° (Found: C, 34·3; H, 2·6%).

The endo-exo-*methanesulphonate* (IX; R = SO_2Me) (from chloroform–light petroleum), m. p. 177—179° (decomp.) (Found: C, 34·4; H, 2·8; S, 6·9%).

The half-cage endo-*methanesulphonate* (XII; R = SO_2Me), needles (from chloroform–light petroleum), changing gradually to rhombs, m. p. 150—152° (decomp.) (Found: C, 33·9; H, 2·6; S, 6·4%).

Solvolysis of the Sulphonates.—The appropriate methanesulphonate (*ca.* 1·3 g.) was refluxed for 18 hr. in acetic acid (20 ml.) containing sodium acetate (5 g. in 100 ml.). The solution was then poured into water and extracted with chloroform. The extract was successively washed with water, aqueous sodium hydrogen carbonate, and water and dried (Na_2SO_4). The residue after evaporation was chromatographed and the molar percentage yields based on material recovered (*ca.* 90%) are recorded in Table 1. The *endo-exo*-methanesulphonate (IX; R = SO_2Me) was recovered unchanged from the above treatment, which was repeated at 190° in a sealed tube. The half-cage acetate (VI; R = Ac) was stable under the standard conditions. Two new compounds were isolated:

The chlorohydrocarbon (XIII ?) had m. p. 262°, after sublimation in a high vacuum (Found: C, 39·9; H, 2·45; Cl, 57·9. $C_{12}H_6Cl_6$ requires C, 39·5; H, 2·2; Cl, 58·3%); it gave no band around 1600 cm.$^{-1}$.

The endo-*acetate* (XII; R = Ac) was sublimed in a high vacuum for analysis and had m. p. 153—154° (Found: C, 39·8; H, 2·8; Cl, 50·0%), $\nu_{max.}$ 3140 and 1750 cm.$^{-1}$, no band around 1600 cm.$^{-1}$. Basic hydrolysis gave the half-cage *endo*-alcohol (XII; R = H), m. p. 260° (decomp.) after sublimation in a high vacuum (Found: C, 37·7; H, 3·0; Cl, 55·0%).

Oxidation of the endo-*Alcohol* (XII; R = H).—The alcohol (201 mg.) was dissolved in acetic acid (2 ml.), and chromium trioxide (48 mg.) in a few drops of water was added. After 24 hr. water was added and the mixture was extracted with chloroform. The chloroform was washed with water, sodium hydrogen carbonate solution, and water and dried (Na_2SO_4). The product was chromatographed and crystallised from chloroform–light petroleum; it had m. p. 296—298° (Found: C, 38·0; H, 2·35; Cl, 55·7%), $\lambda_{max.}$ 294 mμ (ε 40). The infrared spectrum was identical with that of compound (VII) above.

Analysis of Products from Treatment with Acid.—The compound (1—2 g.) was refluxed for 30 min. in acetic acid (20 ml.) with sulphuric acid (4 ml.) and then worked up as for the solvolyses. The results are recorded in Table 2. Thus was obtained the endo-exo-*acetate* (IX; R = Ac) (from ethanol), m. p. 144—145° (Found: C, 39·9; H, 3·5; Cl, 50·7; Ac, 10·1. $C_{14}H_{12}Cl_6O_2$ requires C, 39·5; H, 3·5; Cl, 50·7; Ac, 10·1%), $\nu_{max.}$ 1730, 1600 cm.$^{-1}$. Basic hydrolysis gave 1α,2β,3β,1,8,9,10,11,11-*hexachlorotetracyclo*[6,2,1,$1^{3,6}$,$0^{2,7}$]*dodeca*-9-*en*-4α-*ol* (*endo-exo*-alcohol; IX; R = H); crystallised from ether–light petroleum, this had m. p. 124—125° (Found: C, 37·5; H, 2·7; Cl, 54·5%). Oxidation with chromium trioxide gave the endo-exo-*ketone* (from ether–light petroleum), m. p. 124—125° (Found: C, 37·5; H, 2·4; Cl, 55·6%), $\lambda_{max.}$ 294 mμ (ε 64), $\nu_{max.}$ 1760, 1600, 1415 cm.$^{-1}$.

Deuterium Experiments.—Sulphur trioxide (6·4 g.) was added slowly to deuterium oxide (4 g.) with cooling and stirring, followed by acetic anhydride (13 ml.). Isodrin (7·3 g.) was added and the mixture was stirred and heated to 120°. After 30 min. it was kept at 90° for a further 90 min. The product was worked up in the usual way. Basic hydrolysis and chromatography gave the cage-compound (IV) (2·64 g.) and half-cage alcohol (VI; R = H) (2·55 g.), m. p. 203° after crystallisation from chloroform (Found: C, 37·6; H and D, 2·6; Cl, 55·6.

[12] Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422.

XUM

$C_{13}H_9Cl_6DO$ requires C, 37·5; H and D, 2·6; Cl, 55·5%), $\nu_{max.}$ 2241, 2255sh cm.$^{-1}$ (C–D). Oxidation of this alcohol as before gave a sample of half-cage ketone (VII) in which no band characteristic of C–D could be detected.

Treatment of Isodrin with Bromine.—Bromine (0·4 ml.) in carbon tetrachloride was added dropwise with stirring to a solution of isodrin (5 g.) in carbon tetrachloride (25 ml.). The solution was left overnight and then washed with a solution of potassium iodide and sodium thiosulphate. After removal of solvent the total product was dissolved in acetone (150 ml.) and refluxed for 1 hr. with an excess of potassium permanganate. Most of the acetone was then evaporated and water and sodium metabisulphate were added. The cage-compound (IV) (2·69 g.) was obtained by chloroform extraction.

The cage-compound (IV) was also obtained when the reaction was repeated in the presence of finely divided calcium carbonate (5 g.).

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THE UNIVERSITY, SOUTHAMPTON. [*Received, September 22nd,* 1960.]

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947. *Tetrahedral Nickel*(II) *Complexes and the Factors Determining Their Formation. Part III.*[1] *Complexes with Triarylphosphines.*

By (MISS) M. C. BROWNING, R. F. B. DAVIES, D. J. MORGAN, L. E. SUTTON, and L. M. VENANZI.

Tri-*p*-tolyl- and tri-*p*-methoxyphenyl-phosphine are shown to form complexes of the type L_2NiX_2 (L = phosphine, and X = Cl, Br, I, and SCN). The halogeno-complexes are paramagnetic and have been assigned pseudo-tetrahedral structure in the solid state; the thiocyanato-complexes are diamagnetic and are probably planar. Spectral evidence indicates that in benzene solutions of the chloro- and bromo-complexes there are small amounts of diamagnetic species in equilibrium with paramagnetic species. The increases in dipole moment on replacement of chloride by bromide and iodide are attributed to expansion of the PNiX bond angles.

IN Part I of this series one of us reported the preparation and properties of some complexes of nickel(II) with triphenylphosphine of the type $(Ph_3P)_2NiX_2$, and it was suggested that the halogeno-complexes of this series had tetrahedral structures.

TABLE 1.

Colour, decomposition points and electric and magnetic dipole moments of triarylphosphine complexes of nickel and cobalt.

Compound ‡	Colour	Decomp. pt.	μ (D)	$\mu_{eff.}$ (B.M.)
$(p\text{-Tol}_3P)_2NiCl_2$	Olive-green	203—205°	6·2	3·27
$(p\text{-Tol}_3P)_2NiBr_2$	Dark green	236—238	8·6	3·28
$(p\text{-Tol}_3P)_2NiI_2$	Dark brown	230—232	9·8	3·23
$(p\text{-Tol}_3P)_2Ni(SCN)_2$	Red	207—210	2·3	Diamag.
$(p\text{-Anis}_3P)_2NiCl_2$	Brown	165—167	7·4	3·27
$(p\text{-Anis}_3P)_2NiBr_2$	Red-brown	185—187	9·0	3·26
$(p\text{-Anis}_3P)_2NiI_2$	Dark brown	159—160	9·2	3·22
$(p\text{-Anis}_3P)_2Ni(SCN)_2$	Red	187—190	—*	Diamag.
$(p\text{-Anis}_3P)_2Ni(NO_3)_2$	Green	185—189	—*	3·24
$\{(p\text{-Cl}\cdot C_6H_4)_3P\}_2Ni(SCN)_2$	Red	190—195	—*	Diamag.
$(Ph_3P)_2CoCl_2$	Blue	231—232	—†	4·51
$(Ph_3P)_2CoBr_2$	Green	218—219	7·6	4·57
$(Ph_3P)_2CoI_2$	Brown	232—233	9·6	4·73

* Not measured. † Insoluble in benzene. ‡ Tol = C_6H_4Me; Anis = MeO·C_6H_4.

The dipole moments of $(Ph_3P)_2NiX_2$ (X = Br and I) were determined again and found to be 6·8 and 9·0 D, respectively.

[1] Parts I and II, *J.*, 1958, 719; 1961, 2705.

We report here the preparation of complexes of nickel(II) with tri-*p*-tolyl- and tri-*p*-methoxyphenyl-phosphine by the method used for the isolation of the triphenylphosphine analogues. Tri-*p*-chlorophenylphosphine gave only a pure thiocyanate complex and an impure iodo-complex. The complexes now prepared and characterized are listed in Table 1, with their properties.

TABLE 2.

Magnetic susceptibilities of phosphine complexes of nickel.

Compound	$10^6\chi_m$ * (uncorr.)	$10^6\chi_m$ (corr.)	Temp. (°K)	$\mu_{eff.}$ (corr.) B.M.
$(p\text{-Tol}_3P)_2NiCl_2$	3949	4417	292°	3·225
	3839	4307	292	3·185
	4097	4567	292	3·28
	4292	4760	299	3·38
	8100	8568	153	
	11,500	11,968	103	
			Mean	3·27
$(p\text{-Tol}_3P)_2NiBr_2$	4073	4561	292	3·28
	4696	5184	241	
	5853	6341	199	
	6387	6875	176	
	7460	7948	145	
$(p\text{-Tol}_3P)_2NiI_2$	3957	4477	293	3·25
	3761	4281	298	3·21
			Mean	3·23
$(p\text{-Anis}_3P)_2NiCl_2$	4309	4805	292	3·36
	3906	4401	292	3·22
	4007	4502	293	3·26
	4213	4708	293	3·33
	4159	4654	293	3·32
	6719	7714	189	
	10,950	11,445	117	
			Mean	3·27
$(p\text{-Anis}_3P)_2NiBr_2$	3982	4497	293	3·26
	4506	5021	247	
	5170	5685	217	
	6147	6662	176	
	7492	8007	142	
$(p\text{-Anis}_3P)_2NiI_2$	3968	4515	294	3·27
	3720	4267	293	3·18
	5978	6525	180	
	10,310	30,857	117	
			Mean	3·22
$(p\text{-Anis}_3P)_2Ni(SCN)_2$	−479	34	292	Diamag.
	−350	163	219	
	−239	274	199	
	−386	126	173	
	−386	126	148	
$(p\text{-Anis}_3P)_2Ni(NO_3)_2$	4007	4490	290	3·24
	4527	5010	249	
	5199	5682	217	
	6484	6967	133	
	8441	8924	172	
$\{(p\text{-Cl}\cdot C_6H_4)_3P\}_2Ni(SCN)_2$	−312	187·5	291	Diamag.
	−338	161·5	203	
	−293	207	151	

* Braces indicate groups of figures used for plots of temperature dependence.

Thus, the two new series of complexes appear to be similar to their triphenylphosphine analogues.

Their molecular weights could not be determined because the molar solubilities are low in non-donor solvents suitable for such measurements. They were non-electrolytes in nitrobenzene.

The magnetic susceptibility of the paramagnetic complexes follows the Curie–Weiss law over the range 150—290° K (see Table 2). The diamagnetic complexes, however, show the small, temperature-independent paramagnetism found in the compounds of similar type described in Part II.[1] The values of the magnetic moments of the compounds described in the present communication are very similar to those of the corresponding triphenylphosphine complexes, $(Ph_3P)_2NiX_2$ (X = Cl, Br, and I), for which values of $\mu_{eff.}$ of 3·41, 3·27, and 3·28 have been reported.[2]

The visible and ultraviolet spectra of benzene solutions of the triphenyl, tri-*p*-tolyl,

TABLE 3.

Electronic absorption spectra of the triarylphosphine complexes of nickel.

	Solution		Solid	
Compound	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	" Absorbency "
$(Ph_3P)_2NiCl_2$	400	3000	400	1·57
	525—575	sh	570	0·87
	875	76	930	0·92
$(Ph_3P)_2NiBr_2$	425	5200	450	1·65
	570	300	600	1·11
	920	160	950	1·18
$(Ph_3P)_2NiI_2$	425	3200	450	1·70
	475	sh	525—575	sh
	990	400	650—750	sh
			⩾1000	⩾1·25
$(Ph_3P)_2Ni(SCN)_2$	425	2600	460	1·57
			550	sh
$(p\text{-}Tol_3P)_2NiCl_2$	410	2120	440	1·48
	535	205	560	0·82
	900	108	900	0·84
$(p\text{-}Tol_3P)_2NiBr_2$	435	10,000	440	1·58
	580	225	600	1·25
	920	270	960	1·27
$(p\text{-}Tol_3P)_2NiI_2$	460	6100	480	1·8
	975	570	625—675	1·06
			⩾1000	⩾1·22
$(p\text{-}Tol_3P)_2Ni(SCN)_2$	420	8500	400—420	1·74
			475—525	sh
$(p\text{-}Anis_3P)_2NiCl_2$	440	7400	350	1·55
	550	194	460	1·65
	890	158	540—580	sh
			900	0·875
$(p\text{-}Anis_3P)_2NiBr_2$	465	5000	340	1·61
	585	200	480	1·79
	900	255	575—625	sh
			935	0·92
$(p\text{-}Anis_3P)_2NiI_2$	475	4700	350	1·65
	650—700	sh	515	1·86
	960	520	625—675	sh
			⩾1000	⩾1·19
$(p\text{-}Anis_3P)_2Ni(SCN)_2$	420	14,680	330	1·46
			400	1·43

and tri-*p*-methoxyphenyl derivatives in the region 300—1000 mμ are recorded in Table 3. They are all very similar, the spectra of the tri-*p*-tolylphosphine complexes being typical, (see Fig. 1).

All the paramagnetic complexes show absorption bands at about 900 mμ, characteristic of high-spin complexes of this type, as discussed in Part II.[1] The bands at about 600 mμ in the paramagnetic complexes have extinction coefficients, $\varepsilon_{max.}$, of about 200, while in the diamagnetic complexes, *e.g.*, $(Et_3P)_2NiX_2$, these bands have extinction coefficients of about 600. The absorption spectra of $(Ph_3P)_2NiCl_2$ and of $(Ph_3P)_2Ni(SCN)_2$ in benzene solution are to be taken as being indicative only: the compounds are sparingly soluble in the solvent and thus the extinction coefficients may be in error by a factor of two. The

[2] Cotton, Faut, and Goodgame, *J. Amer. Chem. Soc.*, 1961, **83**, 344.

spectra of the triarylphosphine derivatives differ from those of their butyldiphenylphosphine analogues in that no major shifts of absorption bands are observed in going from benzene solutions to solids (see Table 3).

In Part II it was observed that, for a given anionic ligand, a change from trialkyl- to dialkylphenyl- to alkyldiphenyl-phosphine caused small shifts in the absorption bands of the diamagnetic complexes. Large shifts were observed when either the change of phosphine or the change in physical state was accompanied by a change in magnetic susceptibility. Thus major band shifts were observed on comparing the solid complexes $(Bu^n{}_2PhP)_2NiX_2$, which are diamagnetic, with the solid complexes $(Bu^nPh_2P)_2NiX_2$, which

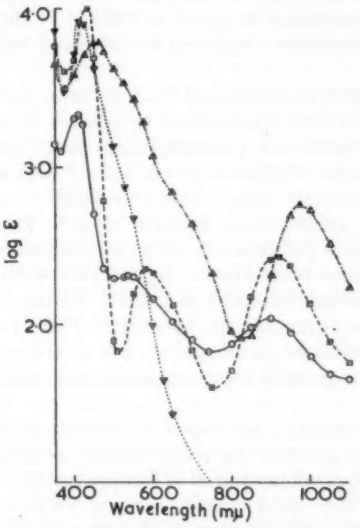

FIG. 1. Spectra of $(p\text{-Tol}_3P)_2NiX_2$ in benzene solution.

—⊙—⊙— X = Cl. –⊡–⊡– X = Br. – · △ – · – △ · – X = I. · · · ▽ · · · ▽ · · · X = SCN.

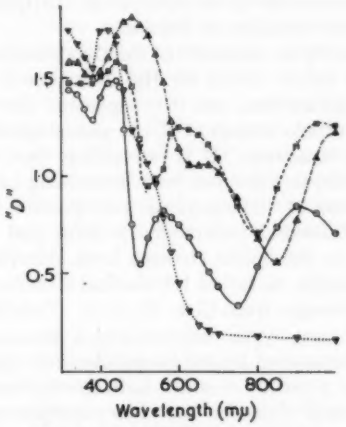

FIG. 2. Reflection spectra of $(p\text{-Tol}_3P)_2NiX_2$.

—⊙—⊙— X = Cl. –⊡–⊡– X = Br. – · △ – · – △ · – X = I. · · · ▽ · · · ▽ · · · X = SCN.

are paramagnetic. Band shifts were also observed between the solid complexes $(Bu^nPh_2P)_2NiX_2$ and their benzene solutions and it was shown that these shifts could be associated with the presence in solution of the equilibrium:

$$\underset{\text{Diamagnetic}}{(Bu^nPh_2P)_2NiX_2} \rightleftharpoons \underset{\text{Paramagnetic}}{(Bu^nPh_2P)_2NiX_2}$$

From magnetic-susceptibility measurements the benzene solutions of $(Bu^nPh_2P)_2NiX_2$, where X = Cl, Br, or I, appear to contain 90%, 40%, and 10%, respectively, of diamagnetic species, and the ratio of the intensities of the band at *ca.* 600 mμ (which is the superimposition of the bands of the diamagnetic and the paramagnetic complex in this region) and that at about 900 mμ (which is characterisic of the paramagnetic species) are in good agreement with the figures quoted above.[1]

The spectroscopic evidence presented here indicates that equilibria of the above type are set up in the triarylphosphine complexes. This hypothesis is supported by the relative intensities of the bands at about 600 and 900 mμ. In the spectra of the solid complexes $(Bu^nPh_2P)_2NiX_2$ and $(Ar_3P)_2NiX_2$ (X = Cl, Br, or I), which are fully paramagnetic, the two bands have intensities which are roughly equal. The intensities of

XUM

the 600 and the 900 mμ bands of the triarylphosphine complexes in benzene solution differ slightly, indicating that small amounts of diamagnetic species may be present in solutions of the chloro- and possibly even of the bromo-complexes (compare Figs. 1 and 2). Confirmation of these conclusions, by measuring the magnetic susceptibility of benzene solutions, is being undertaken by Dr. R. J. P. Williams and co-workers.

There are no apparent shifts in absorption bands of the nickel complexes caused by the substituents in the benzene rings. Thus, the expected changes of strength of the crystal field produced by the operation of the inductive and mesomeric effects of the substituents introduced in *para*-position to the phosphorus atom are very small.

Dipole Moments.—The values of the dipole moments of the triphenylphosphine complexes and of the other triaryl derivatives investigated are given in Table 1. The dipole moments of the chloro-complexes of triphenylphosphine could not be measured because of their low solubility in benzene.

The dipole moments of the thiocyanate complexes are around 2—3 D: these are similar to the values found for the diamagnetic halide and thiocyanate complexes of dibutylphenylphosphine, and it is suggested that they also have a square-planar structure. The larger dipole moments of the paramagnetic halide complexes are in accord with a tetrahedral structure. It is interesting that, contrary to expectation, the dipole moment of the molecule increases with increasing atomic weight of the halogen atom.[3] Two interpretations of this observation are possible: (*a*) an equilibrium is set up in solution between the tetrahedral paramagnetic form and a *trans*-square-planar diamagnetic form which varies as the halide changes from chloride, through bromide, to iodide; (*b*) the complex has a single, distorted tetrahedral structure in solution and the bond angle PNiX increases as X changes from Cl to Br to I. Possible variations in magnetism are explained in the second case by the existence of a paramagnetic ground state and a diamagnetic excited state, separated by only a small energy gap.[1]

The presence of some diamagnetic form in solution, previously suggested on the basis of spectral data for the chloro-complexes and possibly for some bromo-complexes, fits both interpretations. The crystallographic work of Garton *et al.*[4] supports the second: they find that in crystalline $(Ph_3P)_2NiCl_2$ the bond angles are: $\angle PNiP = 116\frac{1}{2}°$, $\angle ClNiCl = 123\frac{1}{2}°$, and $\angle PNiCl = 104°$ and 105°: the structure is thus that of a flattened tetrahedron.[4] If this structure persists in solution then an increase in the size of the halogen atoms will increase the angle PNiX, which is small, and the structure will approach that of a regular tetrahedron.

One of the Referees suggested that the changes in dipole moments observed in the set of compounds $(p\text{-}Tol_3P)_2NiX_2$ cannot be accounted for only on the basis of changes of bond angles and invited us to express our views on this point. We suggest that part of the change might be attributed to increases in bond moments Ni–X in the order Cl < Br < I, due to an increase in polarizability of metal–halogen bonds. A rough calculation, with bond polarizabilities derived from group and atom refractions, and covalent atomic radii with tetrahedral angles, gives the induced moment along the main axis of the molecule caused by the phosphorus–metal dipole acting upon the polarizable metal–halogen bonds. We made one further assumption that the mean dielectric constant of the space between the inducing dipole and the polarizable material was equal to that of benzene. This assumption is scarcely justifiable, though it is probably less bad than assuming a vacuum. The result of this calculation is as follows: for every unit of 1 D in the phosphorus–metal bond, 0·6 D is induced along the main axis between the two metal–halogen bonds, in the case of the bromides (with nickel as the metal); for the iodides the figure is 1·0 D. Of course, to obtain a gross moment we should have to add to this both the values of the unperturbed bond moments and the back-polarization of the phosphorus–metal bond. In view of the crudity of the assumptions, it seems valueless to refine this

[3] Smyth, "Dielectric Behaviour and Structure," McGraw Hill, New York, 1955, p. 244.
[4] Garton, Henn, Powell, and Venanzi, unpublished work.

calculation: nevertheless, it does appear that the observed differences might—in part at least—be explained by this effect.

The dipole moments of two cobalt complexes investigated (which are expected to have tetrahedral structure) are given in Table 1; they show the same increase on replacement of bromide by iodide as the nickel complexes do. Cobalt(II) complexes of this type are not expected to show magnetic variations similar to those of the nickel complexes and so interpretation (*a*) cannot apply here. By analogy it seems likely that the variation in bond angles proposed in (*b*) occurs in the nickel complexes as well as in the cobalt complexes.

The increment in dipole moment produced by the replacement of triphenylphosphine by tri-*p*-tolylphosphine, 1·8 D in L_2NiBr_2 and 0·8 D in L_2NiI_2, calls for comment. A calculation, in which the group moment of the methyl group and regular tetrahedral angles at the phosphorus and nickel atoms are used, predicts an increment in dipole moment of about 0·6 D. Thus, in view of the approximations used in this calculation, the observed and the calculated increment in dipole moment due to the methyl group in the iodide complex are in good agreement. The observed further increment in the bromo-complexes can be explained by assuming that the equilibrium of $(Tol_3P)_2NiBr_2$ in benzene solution contains almost entirely the paramagnetic form while that of $(Ph_3P)_2NiBr_2$ contains some of the diamagnetic form. This is supported by the spectra of the benzene solutions of the two complexes (see Table 3): the ratio of the intensities of the absorption bands at about 600 and 900 mμ are 1 : 1·12 and 1 : 0·55, respectively; ratios of the order 1 : 1 to 1 : 1·2 are normal for fully paramagnetic complexes.

Experimental

Preparation of the Phosphines.—Tri-*p*-tolyl-, tri-*p*-methoxyphenyl-, and tri-*p*-chlorophenylphosphine were prepared by Mann and Chaplin's method.[5] In the preparation of the methoxy-derivative it was preferable to use tetrahydrofuran as solvent.

Preparation of the Complexes.—*Bis(trimethylphosphine)dichloronickel.* The method described in Part I was improved as follows: nickel chloride hexahydrate (2·38 g.) was refluxed for 30 min. with glacial acetic acid (50 c.c.), dehydration being accompanied by a change from green to yellow. The acetic acid was decanted and the residue washed twice with butan-1-ol. A solution of triphenylphosphine (7·80 g.) in butan-1-ol (75 c.c.) was then added to the solid, and the mixture boiled under reflux. The resulting deep blue solution was filtered and, on cooling, the product separated in 86% yield (Found: Ni, 9·0. Calc. for $C_{36}H_{30}Cl_2NiP_2$: Ni, 9·0%).

The following were prepared and purified as described in Part I:

Bis(triphenylphosphine)dibromonickel (Found: Ni, 7·9. Calc. for $C_{36}H_{30}Br_2NiP_2$: Ni, 7·9%). *Bis(triphenylphosphine)di-iodonickel* (Found: Ni, 6·9. Calc. for $C_{36}H_{30}I_2NiP_2$: Ni, 7·0%). *Bis(triphenylphosphine)dithiocyanatonickel* (Found: Ni, 8·4. Calc. for $C_{38}H_{30}N_2NiP_2S_2$: Ni, 8·3%). The tri-*p*-tolyl- and tri-*p*-methoxyphenyl-phosphine complexes were prepared analogously to the corresponding triphenylphosphine complexes. Butan-1-ol was used as a solvent for recrystallization of the complexes unless otherwise specified.

*Bis(tri-*p*-tolylphosphine)dichloronickel* (86%) (Found: Ni, 7·95. $C_{42}H_{42}Cl_2NiP_2$ requires Ni, 8·0%). *Bis(tri-*p*-tolylphosphine)dibromonickel* (55%) (Found: Ni, 6·9. $C_{42}H_{42}Br_2NiP_2$ requires Ni, 7·1%). *Bis(tri-*p*-tolylphosphine)di-iodonickel* (67·5%) (Found: Ni, 6·5. $C_{42}H_{42}I_2NiP_2$ requires Ni, 6·4%). *Bis(tri-*p*-tolylphosphine)dithiocyanatonickel* (69%) (Found: Ni, 7·3. $C_{44}H_{42}N_2NiP_2S_2$ requires Ni, 7·5%). *Bis(tri-*p*-methoxyphenylphosphine)dichloronickel* (73%) (Found: Ni, 7·0. $C_{42}H_{42}Cl_2NiO_6P_2$ requires Ni, 7·0%). *Bis(tri-*p*-methoxyphenylphosphine)dibromonickel* (83·5%) (Found: Ni, 6·2. $C_{42}H_{42}Br_2NiO_6P_2$ requires Ni, 6·4%) *Bis(tri-*p*-methoxyphenylphosphine)di-iodonickel* (81%) (Found: Ni, 5·9. $C_{42}H_{42}I_2NiO_6P_2$ requires Ni, 5·8%). *Bis(tri-*p*-methoxyphenylphosphine)dithiocyanatonickel* (94%) (Found: Ni, 6·95. $C_{44}H_{42}N_2NiO_6P_2S_2$ requires Ni, 6·7%). *Bis(tri-*p*-methoxyphenylphosphine)dinitratonickel* (prepared in 50% yield analogously to the *p*-tolyl derivative) (Found: Ni, 6·55. $C_{42}H_{42}N_2NiO_{12}$ requires Ni, 6·6%). Bis(tri-*p*-chlorophenylphosphine)di-iodonickel (mauve

[5] Mann and Chaplin, *J.*, 1937, 527.

crystals, contaminated with free phosphine) was obtained by the usual method; the mauve product decomposed on attempted recrystallization). *Bis*(*tri*-p-*chlorophenylphosphine*)*dithiocyanatonickel* (90%) (Found: Ni, 6·25. $C_{38}H_{24}Cl_6N_2NiP_2S_2$ requires Ni, 6·5%).

The cobalt complexes were prepared in butan-1-ol solution and recrystallized from the same solvent. The method of preparation is that described for $(Ph_3P)_2NiBr_2$ and gave *bis*(*triphenylphosphine*)-*dichloro*- (74%) (Found: C, 65·8; H, 4·8. $C_{36}H_{30}Cl_2CoP_2$ requires C, 66·1; H, 4·6%), -*dibromo*- (77%) (Found: C, 58·4; H, 4·05. $C_{36}H_{30}Br_2CoP_2$ requires C, 58·2; H, 4·1%), and -*di-iodo-cobalt* (79%) (Found: C, 51·6; H, 3·9. $C_{36}H_{30}CoI_2P_2$ requires C, 51·6; H, 3·6%).

Analysis.—Analysis for nickel was carried out spectrophotometrically by measurement of the absorbance of solutions of the complex obtained by persulphate oxidation of bis(dimethylglyoxime)nickel(II) in the presence of sodium hydroxide, as described in Part II.[1]

Conductance Measurements.—These were carried out on a 0·001M-solution of the complex in nitrobenzene, with a Phillips P.R. 9500 conductivity bridge.

Magnetic Susceptibility Measurements.—These were performed on the finely powdered solids with a Gouy-type balance. The effective magnetic moments, $\mu_{eff.}$, were calculated from the susceptibilities at room temperature, correction being made for the diamagnetism of the component atoms. The susceptibility values are listed in Table 2.

Measurements of Absorption Spectra.—The spectra of the complexes in benzene solution were measured at room temperature on a Beckman ratio recording spectrophotometer (model DK-2) over the range 350—1000 mμ. The complete spectrum was obtained by using 10^{-3}M-solutions for the range 700—1000 mμ, and 10^{-4}M-solutions for the range 350—700 mμ.

The reflection spectra of the finely powdered solids were measured over the range 320—1000 mμ on a Unicam S.P. 500 spectrophotometer fitted with a Unicam diffuse reflection attachment, S.P. 540, magnesium carbonate being the reference standard.

The values of $\lambda_{max.}$ and the corresponding extinction coefficients ε are listed in Table 3.

TABLE 4.

$(Ph_3P)_2NiBr_2$

10^6w_2	ε_{12}	v_{12}
—	2·2750	1·14460
245	2·2768	1·14444
386	2·2777	1·14435
569	2·2792	1·14429

$\varepsilon_{12} = 2{\cdot}2750_6 + 7{\cdot}366w_2$
$v_{12} = 1{\cdot}14461 - 0{\cdot}536w_2$
$_TP_2$ = 1120 c.c.
$_EP_2$ (calc.) = 205 c.c.
$\mu = 6{\cdot}8 \pm 0{\cdot}2$ D

$(Ph_3P)_2NiI_2$

10^6w_2	ε_{12}	v_{12}
—	2·2750	1·14460
350	2·2787	1·14435
442	2·2798	1·14431
476	2·2803	1·14431

$\varepsilon_{12} = 2{\cdot}2749_7 + 10{\cdot}972w_2$
$v_{12} = 1{\cdot}14459 - 0{\cdot}636w_2$
$_TP_2$ = 1852 c.c.
$_EP_2$ (calc.) = 215 c.c.
$\mu = 8{\cdot}95 \pm 0{\cdot}15$ D

$(p\text{-}Tol_3P)_2NiCl_2$

10^6w_2	ε_{12}	v_{12}
—	2·2750	1·14460
501	2·2778	1·14432
642	2·2790	1·14426
691	2·2794	1·14423

$\varepsilon_{12} = 2{\cdot}2749_3 + 6{\cdot}258w_2$
$v_{12} = 1{\cdot}14459 - 0{\cdot}535w_2$
$_TP_2$ = 1001 c.c.
$_EP_2$ (calc.) = 227 c.c.
$\mu = 6{\cdot}2 \pm 0{\cdot}2$ D

$(p\text{-}Tol_3P)_2NiBr_2$

10^6w_2	ε_{12}	v_{12}
—	2·2750	1·14460
288	2·2777	1·14444
692	2·2818	1·14438
828	2·2834	1·14426

$\varepsilon_{12} = 2{\cdot}2749_1 + 10{\cdot}107w_2$
$v_{12} = 1{\cdot}14458 - 0{\cdot}359w_2$
$_TP_2$ = 1766 c.c.
$_EP_2$ (calc.) = 233 c.c.
$\mu = 8{\cdot}6 \pm 0{\cdot}2$ D

$(p\text{-}Tol_3P)_2NiI_2$

—	2·2750	1·14460
382	2·2798	1·14444
508	2·2818	1·14441
738	2·2835	1·14423

$\varepsilon_{12} = 2{\cdot}2752_3 + 11{\cdot}818w_2$
$v_{12} = 1{\cdot}14462 - 0{\cdot}481w_2$
$_TP_2$ = 2278 c.c.
$_EP_2$ (calc.) = 243 c.c.
$\mu = 9{\cdot}8 \pm 0{\cdot}3$ D

$(p\text{-}Tol_3P)_2Ni(SCN)_2$

—	2·2750	1·14460
376	2·2756	1·14444
450	2·2758	1·14444
1450	2·2771	1·14406

$\varepsilon_{12} = 2{\cdot}2750_9 + 1{\cdot}424w_2$
$v_{12} = 1{\cdot}14460 - 0{\cdot}372w_2$
$_TP_2$ = 469 c.c.
$_EP_2$ (calc.) = 242 c.c.
$\mu = 2{\cdot}3 \pm 0{\cdot}2$ D

$(p\text{-}Anis_3P)_2NiCl_2$

—	2·2750	1·14460
577	2·2795	1·14438
863	2·2818	1·14432
1047	2·2833	1·4423

$\varepsilon_{12} = 2{\cdot}2749_3 + 7{\cdot}936w_2$
$v_{12} = 1{\cdot}14459 - 0{\cdot}343w_2$
$_TP_2$ = 1360 c.c.
$_EP_2$ (calc. = 232 c.c.
$\mu = 7{\cdot}4 \pm 0{\cdot}2$ D

$(p\text{-}Anis_3P)_2NiBr_2$

—	2·2750	1·14460
121	2·2662	1·14454
400	2·2785	1·14445
528	2·2808	1·14439

$\varepsilon_{12} = 2{\cdot}2749_3 + 10{\cdot}411w_2$
$v_{12} = 1{\cdot}14458 - 0{\cdot}381w_2$
$_TP_2$ = 1911 c.c.
$_EP_2$ (calc.) = 238 c.c.
$\mu = 9{\cdot}0 \pm 0{\cdot}3$ D

$(p\text{-}Anis_3P)_2NiI_2$

10^6w_2	ε_{12}	v_{12}
—	2·2750	1·14460
117	2·2763	1·14454
230	2·2773	1·14451
685	2·2818	1·14423

$\varepsilon_{12} = 2{\cdot}2750_6 + 9{\cdot}853w_2$
$v_{12} = 1{\cdot}14460 - 0{\cdot}545w_2$
$_TP_2$ = 1968 c.c.
$_EP_2$ (calc.) = 248 c.c.
$\mu = 9{\cdot}2 \pm 0{\cdot}1$ D

$(Ph_3P)_2CoBr_2$

10^6w_2	ε_{12}	v_{12}
—	2·2750	1·14463
200	2·2767	1·14446
295	2·2776	1·14442
357	2·2781	1·14439
759	2·2818	1·14414

$\varepsilon_{12} = 2{\cdot}2749_4 + 8{\cdot}990_5w_2$
$v_{12} = 1{\cdot}1445_8 - 0{\cdot}519w_2$
$_TP_2$ = 1394 c.c.
$_EP_2$ (calc.) = 205 c.c.
$\mu = 7{\cdot}6 \pm 0{\cdot}1$ D

$(Ph_3P)_2CoI_2$

10^6w_2	ε_{12}	v_{12}
—	2·2750	1·14454
200	2·2773	1·14447
355	2·2791	1·14429
361	2·2793	1·14433
476	2·2807	1·14426

$\varepsilon_{12} = 2{\cdot}2749_7 + 11{\cdot}91w_2$
$v_{12} = 1{\cdot}1445_6 - 0{\cdot}638w_2$
$_TP_2$ = 2083 c.c.
$_EP_2$ (calc.) = 215 c.c.
$\mu = 9{\cdot}6 \pm 0{\cdot}1$ D

The intensity of absorption in the reflection spectra is given on an arbitrary scale, " *D*," which may vary from compound to compound.

Dipole-moment Measurements.—These were carried out in benzene solution, and calculated as described in Part I. The experimental data are listed in Table 4.

The authors thank Dr. R. J. P. Williams for the use of a magnetic-suceptibility balance and a Beckman spectrophotometer, Miss M. I. Christie for the use of a Unicam spectrophotometer, and Mr. M. Hely Hutchinson for the measurements of dipole moments of the cobalt complexes.

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948. *The Cross-linking of Cellulose and its Derivatives. Part IV.*[1] *The Action of Hydrazine on the Toluene*-p-*sulphonates of Di*-O-*isopropylidene*-D-*galactose and* -D-*fructose.*

By W. M. CORBETT and D. WINTERS.

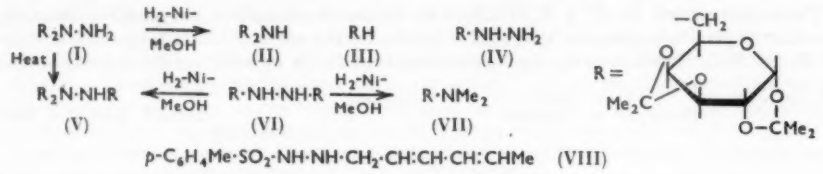
With anhydrous hydrazine, di-*O*-isopropylidene-6-*O*-toluene-*p*-sulphonyl-D-galactose gives, in addition to the known 6-deoxy-6-hydrazinodi-*O*-isopropylidene-D-galactose and hydrazono-6,6′-di-(6-deoxydi-*O*-isopropylidene-D-galactose), the corresponding symmetrical derivative and the reduction product di-*O*-isopropylidene-D-fucose. Similarly, di-*O*-isopropylidene-1-*O*-toluene-*p*-sulphonyl-D-fructose gives 1-deoxy-1-hydrazinodi-*O*-isopropylidene-D-fructose and 1-deoxydi-*O*-isopropylidene-D-fructose, but no bis-derivative has been isolated. The hydrazine derivative of fructose undergoes addition to di-*O*-isopropylidene-D-glucose 3-crotonate, giving 1-deoxydi-*O*-isopropylidene-1-(3-methyl-5-oxopyrazolidin-1-yl)-D-fructose.

A CONVENIENT method was required for the introduction of free amino-groups into cellulose for its cross-linking by addition of an aminocellulose to cellulose crotonate as described in Part I.[2] This has been achieved by 2-cyanoethylation of ethyl cellulose (D.S. *ca.* 2) followed by reduction of the cyano-group,[3] but that method leads to long cross-links. Efforts have therefore been made to develop methods for conversion of 6-*O*-toluene-*p*-sulphonyl-D-glucose repeating units in cellulose toluene-*p*-sulphonate into 6-amino-6-deoxy-D-glucose repeating units which will give shorter cross-links. Replacement of the sulphonic ester groups occurs only to a limited extent with ammonia, but more readily with anhydrous hydrazine to give hydrazino-derivatives.[4] Wolfrom and his co-workers[5] treated several carbohydrate toluene-*p*-sulphonates with hydrazine and reduced the products, which were not isolated, to the amino-derivatives, but yields were not high, indicating that side reactions occur. Such side reactions with cellulose toluene-*p*-sulphonate would lead to repeating groups other than those of 6-amino-6-deoxyglucose and glucose. The possible structure of such groups has been established by a study of the action of hydrazine on the toluene-*p*-sulphonates of di-*O*-isopropylidene-D-galactose and -D-fructose.

Some decomposition of the carbohydrate occurred when the D-galactose derivative was heated with hydrazine at 150° for 20 hr. The hydrazine also decomposed giving ammonia, and among the other volatile products was a thiol (detected by smell only), indicating some reduction of the sulphonate. In addition to the asymmetrical hydrazine (I) described

[1] Part III, Corbett and McKay, *J.*, 1961, 2930.
[2] Corbett and McKay, *J. Soc. Dyers and Colourists*, in the press.
[3] Corbett, unpublished work; cf. *J.*, 1961, 2926.
[4] Freudenberg and his co-workers, (*a*) *Ber.*, 1922, **55**, 3233; *Ber.*, 1923, **56**, (*b*) 1243, (*c*) 2119.
[5] Wolfrom and his co-workers, *J. Amer. Chem. Soc.*, 1958, **80**, 4885; 1959, **81**, 3716; Armstrong, Ph.D. Thesis, Ohio State University, 1958.

by Freudenberg and Hixon,[4c] a new disubstituted derivative was isolated from the water-insoluble fraction. Di-*O*-isopropylidene-D-fucose (III) was also obtained, but in very low yield, and must result from reductive hydrolysis of the toluene-*p*-sulphonyl group by the hydrazine or its decomposition products (cf. the action of lithium aluminium hydride [6]).



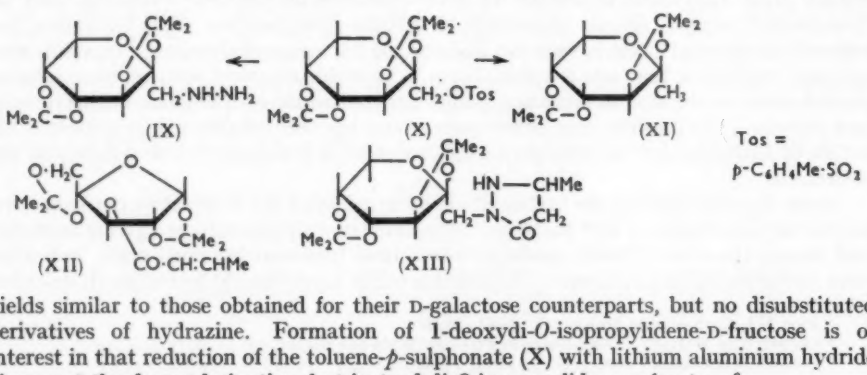
p-$C_6H_4Me\cdot SO_2\cdot NH\cdot NH\cdot CH_2\cdot CH{:}CH\cdot CH{:}CHMe$ (VIII)

From the water-soluble fraction was isolated further di-*O*-isopropylidene-D-fucose and also 6-deoxy-6-hydrazinodi-*O*-isopropylidene-D-galactose (IV) though this could not be obtained free from the fucose derivative (possibly produced by thermal decomposition of the hydrazine derivative). The syrupy hydrazine derivative gave the known crystalline bisphenylcarbamate.[4c]

Decomposition of the sugar and hydrazine also occurred when the reaction mixture was heated for only 5 hr. Again the vapours contained a thiol as well as ammonia, and the same compounds were isolated in similar yields to those in the 20 hr. reaction. The aqueous phase was extracted with ether and concentrated to a dark syrup which on treatment with toluene-*p*-sulphonyl chloride gave a crystalline compound whose elemental analysis and infrared spectrum correspond to those of a *N*-toluene-*p*-sulphonyl derivative of an unsaturated aliphatic hydrazine such as the compound (VIII). Such a compound must arise from decomposition of the sugar portion.

The new bis(di-*O*-isopropylidene-D-galactose) derivative of hydrazine showed no NH stretching or deformation bands in the infrared region, and is therefore the symmetrical molecule (VI). This structure was confirmed by catalytic reduction of the compound in methanol at 150° to 6-deoxy-6-dimethylaminodi-*O*-isopropylidene-D-galactose (VII) whereas the asymmetrical derivative gave the secondary amine (II). In addition to the di-*N*-methyl derivative (VII), hydrogenation of the symmetric hydrazine derivative gave a further new compound which, from its analysis and molecular weight, is believed to be the trisubstituted hydrazine (V): this was also obtained when a dibutyl ether solution of the asymmetrical derivative (I) was refluxed, and must arise from thermal rearrangement.

2,3:4,5-Di-*O*-isopropylidene-1-*O*-toluene-*p*-sulphonyl-D-fructose (X), when heated with hydrazine for 20 hr. gave the hydrazino-derivative (IX) and the deoxy-derivative (XI) in



yields similar to those obtained for their D-galactose counterparts, but no disubstituted derivatives of hydrazine. Formation of 1-deoxydi-*O*-isopropylidene-D-fructose is of interest in that reduction of the toluene-*p*-sulphonate (X) with lithium aluminium hydride gives, not the deoxy-derivative, but instead di-*O*-isopropylidene-D-fructose.[6]

[6] Schmid and Karrer, *Helv. Chim. Acta*, 1949, **32**, 1371.

1-Deoxy-1-hydrazinodi-*O*-isopropylidene-D-fructose with di-*O*-isopropylidene-D-glucose 3-crotonate (XII) gives a complex mixture. Fractional distillation of the product gave di-*O*-isopropylidene-D-glucose and a syrup from which was isolated a further syrup, probably the pyrazolidone (XIII), formed by addition of the primary amine group to the unsaturated group followed by elimination of di-*O*-isopropylidene-D-glucose. The syrup (? XIII) gave a crystalline toluene-*p*-sulphonate which, because it showed infrared carbonyl absorption at *ca.* 1730 cm.$^{-1}$, must be the *N*-derivative and not the *O*-derivative arising from the tautomeric form.

Experimental

Treatment of 1,2:3,4-*Di*-O-*isopropylidene*-6-O-*toluene*-p-*sulphonyl*-D-*galactose with Hydrazine.*—The toluene-*p*-sulphonate (16 g.) was heated with anhydrous hydrazine (40 ml.) for 20 hr. during which a pressure of 40 atm. developed. Water was added to the mixture, smelling of ammonia and a thiol, and the residue (4·86 g.) crystallised from dibutyl ether to give hydrazono-6,6′-di-(6-deoxydi-*O*-isopropylidene-D-galactose) (I) (1·95 g.), m. p. 130—131·5° (lit.,[4c] m. p. 129—130°) (Found: C, 55·4; H, 8·1; N, 5·2. Calc. for $C_{24}H_{40}N_2O_{10}$: C, 55·8; H, 7·8; N, 5·4%). From the mother liquor was obtained *hydrazo*-6,6′-*di*-(6-*deoxydi*-O-*isopropylidene*-D-*galactose*) (VI) (0·86 g.), m. p. 159·5—160·5° [Found: C, 55·8; H, 7·4; N, 5·5%; *M* (Rast), 500. $C_{24}H_{40}N_2O_{10}$ requires C, 55·8; H, 7·8; N, 5·4%; *M*, 516]. Concentration of the residual mother liquor gave a basic syrup which was dissolved in ether, washed with dilute sulphuric acid followed by aqueous sodium carbonate, dried, and concentrated to a syrup (0·75 g.). This distilled at 90—95°/0·005 mm. (bath-temp.), to give di-*O*-isopropylidene-D-fucose (0·20 g.), m. p. 31°, $[\alpha]_D^{22}$ −50·3° (*c* 1·43 in chloroform) (lit.,[7] m. p. 37°, $[\alpha]_D$ −52·4°) (Found: C, 58·9; H, 8·3; N, 0·2. Calc. for $C_{12}H_{20}O_5$: C, 59·0; H, 8·2%).

The aqueous reaction mixture was exhaustively extracted with ether, giving a syrup (4·6 g.) which distilled to give fractions (*a*) (1·11 g.), b. p. 66—78°/0·01 mm., and (*b*) (2·02 g.), b. p. 100—102°/0·005 mm. Fraction (*a*) gave further di-*O*-isopropylidene-D-fucose (0·36 g.), m. p. 31°; fraction (*b*) was impure 6-deoxy-6-hydrazinodi-*O*-isopropylidene-D-galactose (Found: C, 54·1; H, 8·3; N, 7·0. Calc. for $C_{12}H_{22}N_2O_5$: C, 52·5; H, 8·0; N, 10·2%). With phenyl isocyanate it gave a bisphenylcarbamate, m. p. 234—235° (lit.,[4c] m. p. 227°) (Found: C, 60·7; H, 6·3; N, 10·8. Calc. for $C_{26}H_{32}N_4O_7$: C, 60·9; H, 6·3; N, 10·9%).

Reaction of the toluene-*p*-sulphonate (20 g.) with anhydrous hydrazine (50 ml.) at 145—150° for 5 hr. gave the same products in similar yield.

Concentration of the ether-extracted aqueous phase gave a dark syrup (9·9 g.). Acetylation of this did not produce a crystalline derivative, but with toluene-*p*-sulphonyl chloride a sample (4·32 g.) gave crystals (2·20 g.) (from alcohol), m. p. 170—171°, $\nu_{max.}$ 1630 cm.$^{-1}$ (double bond), that were possibly a *N*-toluene-*p*-sulphonyl derivative of an unsaturated hydrazine derivative [Found: C, 59·0; H, 6·7; N, 10·4; S, 11·9%; *M* (Rast), 280. Calc. for $C_{13}H_{18}N_2O_2S$: C, 58·8; H, 6·8; N, 10·5; N, 10·5; S, 11·0%; *M*, 266].

Reactions of the Asymmetrical Hydrazine (I).—(a) *Towards heat.* A dibutyl ether solution (10 ml.) of the hydrazine derivative (0·510 g.) was refluxed for 24 hr. Light petroleum (b. p. 40—60°) was added and the solution filtered and concentrated. The residual syrup (0·495 g.) was digested with hot light petroleum (b. p. 40—60°) and the solid filtered off and recrystallised from aqueous ethanol, to give *tri*-(6-*deoxydi*-O-*isopropylidene*-D-*galactose*-6)-*hydrazine* (0·125 g.), m. p. 198·5—200° [Found: C, 57·0; H, 7·4; N, 3·7%; *M* (Rast), 690. $C_{36}H_{58}N_2O_{15}$ requires C, 57·0; H, 7·7; N, 3·7%; *M*, 758].

Concentration of the light petroleum solution gave a syrup (0·278 g.) which in a short-path still at 150°/0·005 mm. afforded a syrup (0·149 g.) absorbing at 1675 cm.$^{-1}$ (Found: C, 58·2; H, 8·3; N, 4·1. Calc. for $C_{16}H_{29}NO_6$: C, 58·1; H, 8·8; N, 4·2%). It may be a compound formed by the action of the thermal decomposition products of dibutyl ether with the sugar hydrazine derivative or its decomposition products.

(b) *Towards lithium aluminium hydride.* When the hydrazine derivative was treated with an excess of lithium aluminium hydride in ether at room temperature or under reflux, only the starting material (in high yield) was recovered.

The hydrazine derivative (0·513 g.), dibutyl ether (10 ml.), and lithium aluminium hydride (0·25 g.) were refluxed together for 19 hr. To the cooled solution was added ethyl acetate

[7] Freudenberg and Raschig, *Ber.*, 1927, **60**, 1633.

followed by water, chloroform, and aqueous sodium potassium tartrate. The aqueous phase was extracted with chloroform and the combined extracts and chloroform phase were dried, treated with charcoal, and concentrated to a syrup (0·368 g.) which partly crystallised from dibutyl ether. The crystals (0·020 g.), after recrystallisation from di-isopropyl ether, had m. p. 122°, undepressed on admixture with the secondary amine (II).

Concentration of the di-isopropyl ether mother liquor gave a syrup which in a short-path still at 100—120°/0·005 mm. afforded a syrup (0·043 g.) which had a complex infrared spectrum and was not identified.

(c) *Towards hydrogen.* The hydrazine derivative (0·983 g.) in absolute methanol (100 ml.) was hydrogenated over Raney nickel (0·5 g.) for 20 hr. at 150°/50 atm. The filtered mixture was concentrated to a syrup (0·885 g.) which crystallised from light petroleum (b. p. 40—60°), giving the secondary amine (0·424 g.), m. p. and mixed m. p. 127—128·5°. The mother liquors were concentrated; in a short-path still at 100—120°/0·005 mm. the residue gave a syrup (0·059 g.) which had a complex infrared spectrum.

Reduction of the Symmetrical Hydrazine (VI).—The derivative, m. p. 153·5—154·5° (0·373 g.), in absolute methanol (50 ml.) was hydrogenated over Raney nickel (0·5 g.) for 20 hr. at 150°/50 atm. The filtered solution was concentrated to a syrup (0·411 g.) which crystallised from dibutyl ether to give tri-(6-deoxydi-*O*-isopropylidene-D-galactose-6)-hydrazine (0·100 g.), m. p. 196·5—198·5°, undepressed upon admixture with the similar product isolated by the action of heat on the asymmetrical hydrazine (I). Concentration of the mother-liquor followed by distillation gave 6-deoxy-6-dimethylaminodi-*O*-isopropylidene-D-galactose (0·307 g.), b. p. 95—100°/0·005 mm. (bath-temp.) (lit.,[8] b. p. 110—115°/2 mm.) (Found: C, 58·9; H, 8·9; N, 4·8. Calc. for $C_{14}H_{25}NO_5$: C, 58·7; H, 8·7; N, 4·9%).

Treatment of 2,3:4,5-*Di*-O-*isopropylidene*-1-O-*toluene*-p-*sulphonyl*-D-*fructose with Hydrazine.*—The toluene-*p*-sulphonate (40 g.) was heated with anhydrous hydrazine (100 ml.) for 20 hr. at 145° during which a pressure of 50 atm. developed. Water (200 ml.) was added to the mixture which was then exhaustively extracted with ether. Evaporation of the ether gave a colourless syrup (13·73 g.) which was distilled to give fractions (*a*) (9·75 g.), b. p. 140—142°/0·005 mm. (bath-temp.) (Found: C, 53·0; H, 8·1; N, 5·8%), and (*b*) (1·34 g.), b. p. 204°/0·005 mm. (bath-temp.) (Found: C, 55·5; H, 7·8; N, 4·5%). Fraction (*a*) was mainly 1-deoxy-1-hydrazinodi-*O*-isopropylidene-D-fructose, and with phenyl isocyanate gave the *bisphenylcarbamate*, m. p. 195—197° (Found: C, 60·9; H, 6·4; N, 10·2. $C_{26}H_{32}N_4O_7$ requires C, 60·9; H, 6·3; N, 10·9%). Two fractional distillations of the syrup (3·897 g.) gave 1-*deoxydi*-O-*isopropylidene*-D-*fructose* (0·307 g.), b. p. 105—110°/0·005 mm. (Found: C, 58·7; H, 8·3; N, 0·3. $C_{12}H_{20}O_5$ requires C, 59·0; H, 8·2%).

Addition of 1-*Deoxy*-1-*hydrazinodi*-O-*isopropylidene*-D-*fructose to Di*-O-*isopropylidene*-D-*glucose* 3-*Crotonate.*—A solution of the hydrazine derivative (4·89 g.) and the crotonate (6·19 g.) in absolute ethanol (75 ml.) was kept at room temperature for 3 days, then concentrated to a syrup containing several components. These could not be isolated in pure form by fractional distillation. Some of the fractions crystallised spontaneously, to give di-*O*-isopropylidene-D-glucose in a yield representing 38% hydrolysis of the crotonate.

The addition product (4·106 g.) was shaken for 24 hr. with water (80 ml.). The residue (1·890 g.) was unchanged starting material. Concentration of the aqueous phase gave a syrup (1·964 g.) which was dissolved in aqueous ammonia (100 ml.; *d* 0·9). The solution was kept at room temperature for 18 hr., then concentrated to a syrup which was extracted with hot light petroleum (b. p. 40—60°). Evaporation of the solvent gave a syrup from which was isolated di-*O*-isopropylidene-D-glucose (0·535 g.), m. p. and mixed m. p. 112·5—113·5°. The residual syrup distilled at 170°/0·005 mm. (bath-temp.) to give 1-*deoxydi*-O-*isopropylidene*-1-(3-*methyl*-5-*oxopyrazolidin*-1-*yl*)-D-*fructose* (0·211 g.) (Found: C, 56·2; H, 7·6; N, 6·7. $C_{16}H_{26}N_2O_6$ requires C, 56·2; H, 7·7; N, 8·2%) which with toluene-*p*-sulphonyl chloride in pyridine gave the 2-N-*toluene*-p-*sulphonate*, m. p. 201·5—203° (Found: C, 56·3; H, 6·7; N, 5·5; S, 6·9. $C_{23}H_{32}N_2O_8S$ requires C, 55·7; H, 6·5; N, 5·7; S, 6·5%).

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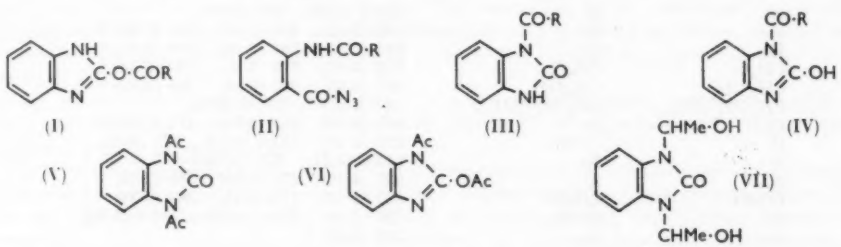
[8] Freudenberg and Smeykal, *Ber.*, 1926, **59**, 100.

949. *Acyl Derivatives of 2-Oxobenzimidazoline.*

By D. Harrison and A. C. B. Smith.

The structures of some mono- and di-acyl derivatives of 2-oxobenzimidazoline have been re-examined and some errors corrected. The ultraviolet and infrared spectra of these compounds are briefly considered.

Monoacetyl and monobenzoyl derivatives of 2-oxobenzimidazoline (2-hydroxybenzimidazole) were prepared by Heller *et al.*[1] by the reaction of the silver salt of 2-oxobenzimidazoline with the corresponding acid chloride, and formulated as (I; R = Me or Ph). We have prepared the same monoacetyl derivative by heating 2-oxobenzimidazoline with acetic anhydride and by thermal decomposition of the azide (II; R = Me) in xylene. The known benzoyl compound was similarly obtained from the benzoyl azide (II; R = Ph), and we conclude that these derivatives are 1-acyl-2-oxobenzimidazolines (III; R = Me or Ph) or the tautomeric 1-acyl-2-hydroxybenzimidazoles (IV). The acyl azides (II) were prepared by the action of the acid chloride in pyridine on *o*-aminobenzazide; the benzoyl azide was also prepared from methyl *o*-benzamidobenzoate *via* the hydrazide.



By the action of acetyl chloride in pyridine on 2-oxobenzimidazoline, and in other ways, Heller *et al.*[1] prepared 1,3-diacetyl-2-oxobenzimidazoline (V). The formation of an isomeric compound (VI) by boiling "benzimidazole oxide" with acetic anhydride is also recorded.[2] We have repeated both preparations and obtained identical products. The diacetyl derivative is conveniently prepared by boiling a solution of 2-oxobenzimidazoline in acetic anhydride for a longer time than used in the preparation of the monoacetyl compound. If Heller's formulation is correct, reduction of the diacetyl compound could yield either 1,3-bis-1′-hydroxyethyl-2-oxobenzimidazoline (VII) or 1,3-diethyl-2-oxobenzimidazoline. With lithium aluminium hydride in boiling ether or tetrahydrofuran, the reduction appeared to proceed satisfactorily, but the only isolable product was 2-oxobenzimidazoline. It is not clear whether the N–C bond is broken in the reduction or during the working up. Attempts to prepare the bishydroxyethyl compound (VII) from 2-oxobenzimidazoline and acetaldehyde failed. The corresponding bishydroxymethyl compound is easily prepared,[3] but is decomposed by dilute alkali. 1,3-Diethyl-2-oxobenzimidazoline, whose structure is deduced from a comparison of its ultraviolet and infrared spectra with those of the known 1,3-dimethyl compound, was obtained from 2-oxobenzimidazoline and diethyl sulphate in sodium hydroxide solution, but attempts to oxidise it to a 1,3-diacetyl compound were unsuccessful.

The 1,3-diacyl formulation was finally deduced by the following indirect method. A monopropionyl derivative was prepared from 2-oxobenzimidazoline and assigned a 1-acyl structure on account of the close similarity of its ultraviolet spectrum to that of

[1] Heller, Buchwaldt, Fuchs, Kleinicke, and Kloss, *J. prakt. Chem.*, 1925, **111**, 1.
[2] Montanari and Risaliti, *Gazzetta*, 1953, **83**, 278.
[3] Monti and Venturi, *Gazzetta*, 1946, **76**, 364.

the 1-acetyl compound. On boiling this 1-propionyl derivative with acetic anhydride the acetyl-propionyl compound obtained was identical with that obtained by boiling 1-acetyl-2-oxobenzimidazoline with propionic anhydride. Since under these conditions migration of acyl groups may have occurred, the second acyl group was also introduced by using acetyl or propionyl chloride in cold pyridine, but the result was the same. Hence the acetyl-propionyl compound must have the 1,3-diacyl structure. Since the ultraviolet spectra of the diacetyl, dipropionyl, and acetyl-propionyl compounds are almost identical, it is concluded that these three compounds have similar structures. Experiments of this type were also carried out with acetyl-benzoyl compounds.

The ultraviolet spectra of simple benzimidazoles are characterised in the region 260—290 mμ by a group of three maxima, the first sometimes only appearing as an inflection, but the other two being very sharply marked. Substituents in the 1- and the 2-position leave the basic pattern unchanged.[4,5] The details of the spectra of a number of 1,3-disubstituted 2-oxobenzimidazolines are included in the Table; they show a single broad

Ultraviolet absorption spectra of 2-oxobenzimidazolines in ethanol

1-Subst.	3-Subst.	$\lambda_{max.}$ (mμ) (log ε in parentheses)
H	H	225·5 (3·86); 280 (3·88)
Me	Me	232 (3·82); 283 (3·88); 287 (3·83) *
Et	Et	233 (3·82); 284 (3·88); 288 (3·82) *
CH_2Cl	CH_2Cl	226 (3·88); 279 (3·80); 284 (3·76) *
CH_2·OH	CH_2·OH	227 (3·88); 280 (3·85); 285 (3·80) *
CH_2·N<[CH_2]$_5$	CH_2·N<[CH_2]$_5$	226 (3·87) *; 281·5 (3·84)
H	Ac	220 (4·40); 253 (3·74); 277·5 (3·48)
H	CO·Et	220 (4·40); 251·5 (3·78); 278 (3·56)
H	Bz	244·5 (4·31); 275 (3·78); 283 (3·73) *
Ac	Ac	237 (4·12); 272 (3·36); 280 (3·30)
CO·Et	CO·Et	237 (4·13); 273 (3·41); 281 (3·34)
Ac	CO·Et	236 (4·14); 272·5 (3·38); 280·5 (3·30)
Ac	Bz	247 (4·30)

* Inflection.

maximum near 280 mμ. With diacetyl-2-oxobenzimidazoline, conjugative interaction of the acetyl groups with the ring system complicates the situation, and the spectrum has two broad maxima at 272 and 282 mμ (ε approximately one-third of its value for the reference compounds). Nevertheless, the difference from the benzimidazole-type spectrum supports the 1,3-diacetyl structure.

The infrared spectra of the mono- and the di-acyl-2-oxobenzimidazolines were determined originally to assist in the determination of their structure, but interpretation proved to be difficult. The amide I band in 2-oxobenzimidazoline itself [6] is at an abnormally high frequency compared with that of the 1,3-dimethyl and 1,3-diethyl compounds, and with certain substituted 2-oxoimidazolines.[7] In the spectra of 1-acetyl-2-oxo- and 2-oxo-1-propionyl-benzimidazoline there are two strong bands in the 1700—1750 cm.$^{-1}$ region, but these are probably better regarded as associated with the –CO·N·CO·NH– system as a whole than as separate carbonyl stretching frequencies. A strong band near 3180 cm.$^{-1}$ in these compounds can be assigned to N–H stretching (hydrogen-bonded), but the origin of other bands in this region is less certain since C–H frequencies are possible near 3000 cm.$^{-1}$. The presence of the N–H band is, however, strong evidence against structures such as (IV). The spectra of the 1,3-diacyl compounds contained two or three strong bands between 1700 and 1770 cm.$^{-1}$ but again assignment to specific carbonyl groups is of doubtful validity.

[4] Efros and Eltsov, *Zhur. obschei Khim.*, 1957, **27**, 684.
[5] Leandri, Mangini, Montanari, and Passerini, *Gazzetta*, 1955, **85**, 769.
[6] Harrison and Smith, *J.*, 1959, 3157.
[7] Gompper and Herlinger, *Chem. Ber.*, 1956, **89**, 2825.

Experimental

Infrared spectra were determined in potassium bromide discs, and only strong bands in the regions 1650—1800 cm.$^{-1}$ and 3000—3500 cm.$^{-1}$ are recorded.

o-*Acetamidobenzazide*.—Acetyl chloride (0·4 ml.) was added to a stirred solution of *o*-aminobenzazide [8] (0·65 g.) in pyridine (1·5 ml.). After 15 min., addition of water (10 ml.) precipitated a solid which was collected, washed with water, and dried *in vacuo* (0·63 g., 77%). Recrystallisation from ethanol (N.B. overheating must be avoided) gave o-*acetamidobenzazide* as colourless needles, m. p. 84—85° (Found: C, 53·0; H, 3·9; N, 27·8. $C_9H_8N_4O_2$ requires C, 52·9; H, 3·95; N, 27·4%).

o-*Benzamidobenzhydrazide*.—A mixture of methyl *o*-benzamidobenzoate (12·7 g.), ethanol (75 ml.), and 98% hydrazine hydrate (15 ml.) was boiled under reflux for 30 min. On cooling, the hydrazide separated as a white solid (10·3 g., 81%); after recrystallisation from ethanol it had m. p. 183—185° (lit.,[9] 176°) (Found: C, 65·8; H, 5·4; N, 16·9. Calc. for $C_{14}H_{13}N_3O_2$: C, 65·9; H, 5·1; N, 16·5%). As the m. p. of the cyclized product 3-amino-3,4-dihydro-4-oxo-2-phenylquinazoline is given as 184—186° [9] and as 178—179°,[10] a mixed m. p. determination was necessary to show that cyclization had not occurred; a depression of 10° was observed.

o-*Benzamidobenzazide*.—(*a*) To a solution of *o*-benzamidobenzhydrazide (5·1 g.) in 1·5N-hydrochloric acid (175 ml.), 10% aqueous sodium nitrite (16 ml.) was added. The gummy precipitate was collected after 30 min., washed with water (4 × 20 ml.), dried, and recrystallised cautiously from ethanol to give o-*benzamidobenzazide* (2·6 g., 48%) as yellow needles, m. p. 108—110° (decomp.) (Found: C, 62·8; H, 4·1; N, 21·3. $C_{14}H_{10}N_4O_2$ requires C, 63·1; H, 3·7; N, 21·0%).

(*b*) By a method similar to that used for *o*-acetamidobenzazide, *o*-aminobenzazide was benzoylated, giving a product, m. p. 108—110° (decomp.) not depressed on admixture with a sample prepared by method (*a*).

1-*Acetyl-2-oxobenzimidazoline*.—(a) *From 2-oxobenzimidazoline*. 2-Oxobenzimidazoline (1 g.) was boiled under reflux for 30 min. with acetic anhydride (6 ml.). After addition of water (20 ml.), further boiling (10 min.), and cooling, the crude product was collected, washed with water (3 × 5 ml.), and dried. Recrystallisation from benzene gave the 1-acetyl derivative (0·74 g., 56%), m. p. 205—207° (lit.,[1] 205°), $\nu_{max.}$ 3180, 3100, 3050, 1740, 1709 cm.$^{-1}$.

(b) *From* o-*acetamidobenzazide*. A solution of the azide (0·07 g.) in xylene (1 ml.) was kept at 100° for 30 min., then cooled, and the solid was collected, washed with ether, and dried, to give 1-acetyl-2-oxobenzimidazoline (0·04 g.), m. p. 204—207°, not depressed by samples prepared either by method (a) above or from the silver salt of 2-oxobenzimidazoline.[1]

2-*Oxo*-1-*propionylbenzimidazoline*.—Modification of the method used for the 1-acetyl compound was necessary in order to avoid extensive dipropionylation. The following procedure gave only moderate yields. 2-Oxobenzimidazoline (5·42 g.), water (4 ml.), and propionic anhydride (33 ml.) were mixed and heated for 15 min. under reflux at 140—150°. More propionic anhydride (5 ml.) was then added and the bath temperature raised to 170—180° for 15 min. Cooling and pouring the mixture into water (300 ml.) afforded a solid of indefinite m. p. This was boiled with benzene (100 ml.), insoluble matter was filtered off, and the filtrate concentrated to give the required *propionyl derivative* (1·37 g., 18%), m. p. 173—175°, raised by recrystallisation from benzene to 181—183°, $\nu_{max.}$ 3180, 3100, 1737, 1716 cm.$^{-1}$ (Found: C, 63·0; H, 5·5; N, 15·0. $C_{10}H_{10}N_2O_2$ requires C, 63·1; H, 5·3; N, 14·7%).

1-*Benzoyl-2-oxobenzimidazoline*.—A solution of *o*-benzamidobenzazide (1·25 g.) in xylene (20 ml.) was boiled under reflux for 30 min. The solid which separated on cooling was washed with ether and recrystallised from benzene, to give 1-benzoyl-2-oxobenzimidazoline (0·84 g., 75%), m. p. 198—200° (lit.,[1] 205°), $\nu_{max.}$ 3190, 3115, 1730, 1692 cm.$^{-1}$. The m. p. was not depressed on admixture with a sample prepared from the silver salt of 2-oxobenzimidazoline.[1]

1,3-*Diacetyl-2-oxobenzimidazoline*.—2-Oxobenzimidazoline (1 g.) was boiled under reflux for 4 hr. with acetic anhydride (6 ml.). On cooling, the diacetyl derivative separated (1·15 g., 71%), forming needles (from ethanol), m. p. 149—151°, $\nu_{max.}$ 1770, 1724 cm.$^{-1}$. Samples were also prepared (*a*) from 2-oxobenzimidazoline and acetyl chloride in pyridine [1] (lit., m. p. 149°)

[8] Heller and Siller, *J. prakt. Chem.*, 1926, **116**, 9.
[9] Hirwe and Kulkarni, *Proc. Indian Acad. Sci.*, 1942, **16**, *A*, 294.
[10] Heller, *Ber.*, 1915, **48**, 1191.

and (*b*) by boiling benzimidazole *N*-oxide [11] with acetic anhydride [2] (lit., m. p. 154—155°). By determinations of mixed m. p. and ultraviolet spectra the samples were shown to be identical.

2-Oxo-1,3-dipropionylbenzimidazoline.—2-Oxobenzimidazoline (1 g.) was heated for 30 min. with propionic anhydride (6 ml.) in a bath at 140—160°. The solid which separated on cooling (1·55 g., 84%) afforded *2-oxo-1,3-dipropionylbenzimidazoline* (needles from ethanol), m. p. 167—169°, $\nu_{max.}$ 1758, 1731, 1718sh cm.$^{-1}$ (Found: C, 63·4; H, 5·8; N, 10·5. $C_{13}H_{14}N_2O_3$ requires C, 63·4; H, 5·7; N, 11·3%).

1-Acetyl-2-oxo-3-propionylbenzimidazoline.—A stirred solution of 1-acetyl-2-oxobenzimidazoline (0·2 g.) in pyridine (3 ml.) was cooled in an ice-bath and treated with propionyl chloride (0·3 ml.). After 10 min., water (15 ml.) was added and the solid collected. Recrystallisation from ethanol gave *1-acetyl-2-oxo-3-propionylbenzimidazoline* (0·14 g., 40%) as colourless needles, m. p. 151—152°, $\nu_{max.}$ 1757, 1733, 1716sh cm.$^{-1}$ (Found: C, 62·3; H, 5·4; N, 11·7. $C_{12}H_{12}N_2O_3$ requires C, 62·1; H, 5·2; N, 12·1%). Samples were also prepared from 2-oxo-1-propionylbenzimidazoline (*a*) by reaction with acetyl chloride in pyridine, and (*b*) by heating it with acetic anhydride at 130—140° for 1 hr. The three samples were shown to be identical in the usual way.

1-Acetyl-3-benzoyl-2-oxobenzimidazoline.—The method used for the 1-acetyl-3-propionyl compound, but with benzoyl chloride in place of propionyl chloride, afforded *1-acetyl-3-benzoyl-2-oxobenzimidazoline* (needles from ethanol), m. p. 167—169°, $\nu_{max.}$ 1759, 1720, 1707 cm.$^{-1}$ (Found: C, 68·6; H, 4·3; N, 9·9. $C_{16}H_{12}N_2O_3$ requires C, 68·6; H, 4·3; N, 10·0%). An identical product was obtained from 1-benzoyl-2-oxobenzimidazoline and acetyl chloride in pyridine.

1,3-Diethyl-2-oxobenzimidazoline.—A mixture of 2-oxobenzimidazoline (5 g.), 10% aqueous sodium hydroxide (40 ml.), and diethyl sulphate (12 ml.) was boiled under reflux for 3 hr. More sodium hydroxide (10 g.) was then added and heating continued for a further 30 min. Addition of water (75 ml.) and extraction with benzene (3 × 50 ml.) furnished an oil (4·43 g., 62·4%). This was distilled, and the fraction of b. p. 92—100°/0·3 mm. crystallised. Recrystallisation from light petroleum (b. p. 60—80°) gave *1,3-diethyl-2-oxobenzimidazoline*, m. p. 67—71°, $\nu_{max.}$ 1693 cm.$^{-1}$ (Found: C, 69·4; H, 7·4; N, 14·5. $C_{11}H_{14}N_2O$ requires C, 69·5; H, 7·4; N, 14·7%).

Other Compounds.—The following were prepared by recorded methods:

1,3-Dimethyl-2-oxobenzimidazoline, m. p. 107—109° (lit.,[12,13] 107·5° and 106·5—107°), $\nu_{max.}$ 1690 cm.$^{-1}$.

1,3-Bishydroxymethyl-2-oxobenzimidazoline, m. p. 156—159° (lit.,[3,13] 164—165° and 165°). The unexpected solubility of this compound in dilute aqueous sodium hydroxide, noted by Monti and Venturi,[3] was confirmed. It is probably due to reversible decomposition into formaldehyde and 2-oxobenzimidazoline, since the ultraviolet spectrum of the hydroxymethyl compound in 0·1N-sodium hydroxide was identical with that of 2-oxobenzimidazoline in the same solvent.

1,3-Bischloromethyl-2-oxobenzimidazoline, m. p. 168—171° [lit.,[13] 167° (decomp.)].

2-Oxo-1,3-bispiperidinomethylbenzimidazoline, m. p. 125—127° (lit.,[13] 125°).

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[11] Niementowski, *Ber.*, 1910, **43**, 3012.
[13] Zinner and Spangenburg, *Chem. Ber.*, 1958, **91**, 1433.
[13] Efros, Poras-Koshits, and Farbenstein, *Zhur. obschei Khim.*, 1953, **23**, 169.

950. *Carbohydrate Components of Antibiotics. Part I. Degradation of Desosamine by Alkali: its Absolute Configuration at Position 5.*

By C. H. Bolton, A. B. Foster, M. Stacey, and J. M. Webber.

Alkaline degradation of desosamine, a 3,4,6-trideoxy-3-dimethylaminohexose, yields (*erythro* + *threo*)-2,5-dihydroxyhexanoic acid. This acid is further degraded to (−)-pentane-1,4-diol containing the asymmetric carbon atom which was originally $C_{(5)}$ of desosamine. The absolute configuration of (−)-pentane-1,4-diol is correlated with that of D-glyceraldehyde, thereby indicating that desosamine is a D-hexose derivative.

Several 3-deoxy-3-dimethylaminohexose derivatives have now been recognised as structural components of antibiotics. Desosamine (picrocin), a 3,4,6-trideoxy-3-dimethylaminohexose, forms part of the macrolide antibiotics erythromycin,[1] methymycin,[2] narbomycin,[3] oleandomycin,[4] and picromycin.[5] Carbomycin (magnamycin),[6] also a macrolide antibiotic, contains mycaminose, a 3,6-dideoxy-3-dimethylaminohexose. Amosamine, present in amicetin,[7] is probably [8,9] also a 3,6-dideoxy-3-dimethylaminohexose; amosamine and mycaminose exhibit markedly different mobilities in paper chromatography.[9] Rhodomycin [10] contains rhodosamine which is believed to be a 2,3,6-trideoxy-3-dimethylaminohexose. Although a partial relative configuration has been deduced for mycaminose,[11] its absolute configuration, and that of the other 3-deoxy-3-dimethylaminohexose derivatives, have not been established. We now report a partial configurational assignment for desosamine.

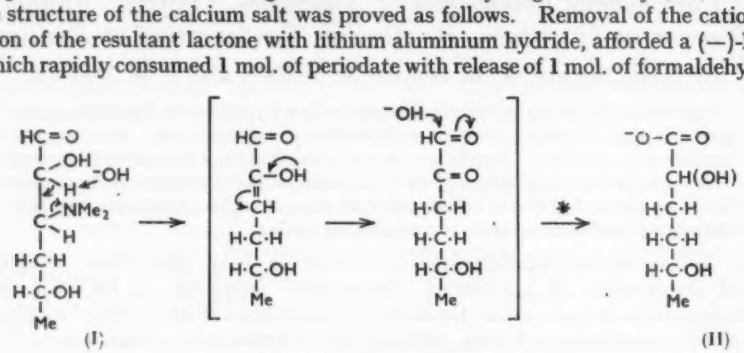
Allocation of the skeletal structure of desosamine (and of the other 3-deoxy-3-dimethylaminohexose derivatives) is based mainly on the pattern of periodate oxidation [12,13] and on the ease of elimination of dimethylamine during treatment with alkali.[13] The other products of the latter reaction, which is indicative [6] of a β-amino-carbonyl structure, have apparently not been identified although a mechanism has been postulated [11] for the alkaline degradation of mycaminose. Identification of the products in the case of desosamine has now permitted both determination of the absolute configuration at position 5 and confirmation of the skeletal structure.

Desosamine hydrochloride was readily isolated in *ca.* 60% yield after vigorous acidic hydrolysis of erythromycin. Dimethylamine (91% in *ca.* 24 hr.) was evolved when the sugar was treated with 0·05N-sodium hydroxide at 50°. When the degradation was performed with oxygen-free lime water at 25°, 6—7 days were required for complete reaction. The same acidic product (isolated as the calcium salt) was formed in each degradation and, by analogy with the products of the alkaline decomposition of 3-*O*-substituted hexoses,[14] it was expected to be calcium (*erythro* + *threo*)-2,5-dihydroxyhexanoate arising by the mechanism [11] (I) ⟶ (II). An alternative mechanism analogous

[1] Clark, *Antibiotics and Chemotherapy*, 1953, **3**, 663; Wiley, Gerzon, Flynn, Sigal, Weaver, Quarck Chauvette, and Monahan, *J. Amer. Chem. Soc.*, 1957, **79**, 6062.
[2] Djerassi and Zderic, *J. Amer. Chem. Soc.*, 1956, **78**, 6390; Djerassi and Halpern, *ibid.*, 1957, **79**, 2022.
[3] Corbaz, Ettlinger, Gäumann, Keller, Kradolfer, Kyburz, Neipp, Prelog, Reusser, and Zähner, *Helv. Chim. Acta*, 1955, **38**, 935.
[4] Els, Celmer, and Murai, *J. Amer. Chem. Soc.*, 1958, **80**, 3777.
[5] Brockmann and Oster, *Chem. Ber.*, 1957, **90**, 605; Anliker and Gubler, *Helv. Chim. Acta*, 1957, **40**, 119.
[6] Hochstein and Regna, *J. Amer. Chem. Soc.*, 1955, **77**, 3353.
[7] Stevens, Gasser, Mukherjee, and Haskell, *J. Amer. Chem. Soc.*, 1956, **78**, 6212.
[8] Professor C. L. Stevens, personal communication.
[9] Foster, Lehmann, Webber, and Westwood, unpublished results.
[10] Brockmann and Borchers, *Chem. Ber.*, 1953, **86**, 261; Brockmann and Spohler, *Naturwiss.*, 1955, **42**, 154.
[11] Woodward, *Angew. Chem.*, 1957, **69**, 50.
[12] Flynn, Sigal, Wiley, and Gerzon, *J. Amer. Chem. Soc.*, 1954, **76**, 3121.
[13] Brockmann, König, and Oster, *Chem. Ber.*, 1954, **87**, 856.
[14] Whistler and BeMiller, *Adv. Carbohydrate Chem.*, 1958, **13**, 289.

to that given [15] for the alkaline degradation of 3-*O*-methyl-D-glucose may also be invoked.

The structure of the calcium salt was proved as follows. Removal of the cations, and reduction of the resultant lactone with lithium aluminium hydride, afforded a (—)-hexanetriol which rapidly consumed 1 mol. of periodate with release of 1 mol. of formaldehyde, and



(I) (II)

* Benzilic acid rearrangement.

therefore contained the ·CH(OH)·CH_2·OH grouping with the third hydroxyl group not vicinal. The (—)-hexanetriol had mobilities in paper chromatography, and in ionophoresis in a borate buffer at pH 10, similar to those of hexane-1,2,6-triol, but the two triols were chemically different. That the (—)-hexanetriol contained an unbranched carbon chain, and a 1,2,5-, not a 1,2,4-, distribution of the hydroxyl groups, followed from the isolation of (—)-pentane-1,4-diol on reduction, with borohydride, of the products of periodate oxidation. Two lines of evidence indicated a 1,4-distribution of the hydroxyl groups in the optically active diol. First, the diol did not form a complex with borate ions as shown by the zero M_G value in paper ionophoresis in alkaline borate, behaviour characteristic of 1,4-diols whereas hexane-1,2,4-triol would have been degraded to pentane-1,3-diol and Frahn and Mills [16] have found several acyclic 1,3-diols to have M_G values in the range 0·05—0·24. Secondly, a *ca.* 0·004M-solution of the (—)-pentanediol in carbon tetrachloride had $\nu_{max.}$ at 3634 (ε 33) and 3479 cm.$^{-1}$ (ε 15) for free and intramolecularly bonded hydroxyl groups,[17] respectively, an absorption pattern closely similar to that of butane-1,4-diol [18] [$\nu_{max.}$ 3640 (ε 29) and 3484 cm.$^{-1}$ (ε 11)]. The $\Delta\nu$ values [17] for these diols (155 and 156 respectively) are characteristic of intramolecular hydrogen bonds in 1,4-diols and quite different from those [18] for comparable 1,2- and 1,3-diols (*e.g.*, ethane-1,2-diol $\Delta\nu$ 26, and propane-1,3-diol $\Delta\nu$ 76). Since the (—)-pentane-1,4-diol and authentic racemic pentane-1,4-diol gave indistinguishable infrared spectra (liquid films) the identity of the former compound was established. Racemic pentane-1,4-diol was readily obtained by the reduction of lævulic acid with lithium aluminium hydride.

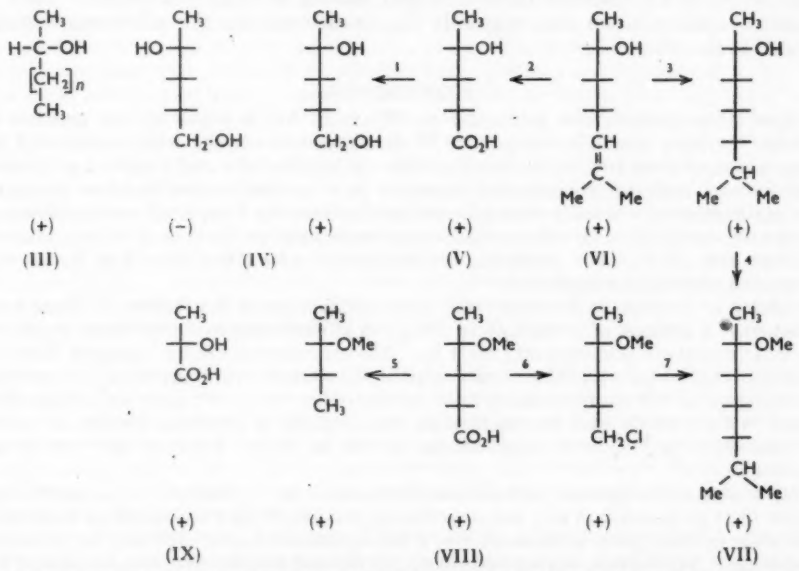
The (—)-hexane-1,2,5-triol gave a tri-(*p*-phenylazobenzoate) with a diffuse melting point which was not sharpened by repeated recrystallisation. This is strong evidence for the presence of a mixture of *erythro*- and *threo*-isomers, since *p*-phenylazobenzoates of pure and racemic alcohols generally exhibit well-defined melting points.[19] Further relevant examples are (—)-pentane-1,4-diol and the racemic alcohols, hexane-1,2,6-triol and pentane-1,4-diol, all of which gave sharp melting *p*-phenylazobenzoates. It follows that the immediate precursor of the (—)-hexane-1,2,5-triol was (*erythro* + *threo*)-2,5-dihydroxyhexanoic acid. No evidence was obtained which indicated the proportions of isomers in this product. The formation of isomers is more easily demonstrated in the alkaline degradation of mycaminose. Reduction with sodium borohydride [20] of the lactone isolated

[15] Kenner and Richards, *J.*, 1954, 278.
[16] Frahn and Mills, *Austral. J. Chem.*, 1959, **12**, 65.
[17] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.
[18] Foster, Haines, and Stacey, *Tetrahedron*, in the press.
[19] Baggett, Foster, Haines, and Stacey, *J.*, 1960, 3528.
[20] Wolfrom and Wood, *J. Amer. Chem. Soc.*, 1951, **73**, 2933; Wolfrom and Anno, *ibid.*, 1952, **74**, 5583.

after the alkaline degradation gave a mixture of 3,6-dideoxy-*arabino*- and -*ribo*-hexose, easily separable by paper ionophoresis in an alkaline borate buffer.[21] It is of interest that the proportion of isomers in the mixture of α- and β-D-glucometasaccharinic acids formed by the alkaline degradation of 3-*O*-benzyl-D-glucose varies according to the experimental conditions.[22] Establishment of the structures of the sequence of products obtained after the alkaline degradation of desosamine also substantiates the structure allocated to the amino-sugar derivative.

Although the yield of dimethylamine from the degradation of desosamine with sodium hydroxide was high (91%), the yield of acidic products was much lower (65%). The difference was accounted for by a second, unidentified, non-acidic product, that was readily separated by chromatography on a cellulose column.

The (—)-pentane-1,4-diol described above contains one asymmetric carbon atom which remained unaffected in the sequence of reactions by which the diol was derived from desosamine. The absolute configuration of (—)-pentane-1,4-diol, which showed a plain negative rotatory dispersion, can be deduced in two ways. First, it is known [23] that compounds having the absolute configuration (III) are dextrorotatory. It is reasonable to suppose that since the hydroxymethyl group in (—)-pentane-1,4-diol is relatively remote



1,* Reduction of acid lactone with sodium and acetic acid.[25] 2, Ozonolysis, followed by oxidation of the resulting aldehyde with silver oxide.[25] 3, Catalytic hydrogenation.[25] 4,* Methylation of potassium alkoxide with methyl iodide.[26] 5,* Bromination decarboxylation of the silver salt, followed by decomposition of the Grignard salt of the product with water.[26] 6, Reduction with lithium aluminium hydride to give (+)-4-methoxypentan-1-ol, followed by treatment with thionyl chloride.[26] 7, Condensation of the Grignard salt with acetone, followed by dehydration, to give (+)-6-methoxy-2-methylhept-2-ene, and catalytic hydrogenation.[26]

For clarity, all stages in this scheme are depicted with (+)-enantiomorphs; stages marked * were actually performed with (—)-enantiomorphs.

from the asymmetric carbon atom it will have little effect on the optical activity. This being so, the (—)-pentane-1,4-diol can be assigned configuration (IV). Secondly, by

[21] Foster, Lehmann, and Stacey, unpublished results.
[22] Machell and Richards, *J.*, 1960, 1938.
[23] Mills and Klyne, "Progress in Stereochemistry," Butterworths Scientific Publ., London, 1954, Vol. I, p. 177; Klyne, "Determination of Organic Structure by Physical Methods," Academic Press Inc., New York, 1955, p. 73.

reference to the literature, a correlation between the configurations of (−)-pentane-1,4-diol and (−)-lactic acid may be established. Levene and Haller [24] resolved 4-hydroxypentanoic acid (V), prepared by reduction of lævulic acid, and correlated the configuration of the dextrorotatory acid with that of (+)-lactic acid (IX). Since further reduction of (−)-(V) gave (−)-pentane-1,4-diol (IV),[25] the latter was assigned the same configuration as (−)-lactic acid. Doering and Young [26] have, however, suggested that several of the stages in Levene's correlations are unreliable because of possible participation by the asymmetric centre in reactions involving a neighbouring group. Consequently, in their investigations, methyl ethers of the secondary alcohol intermediates were employed so that any involvement of the asymmetric centre could be more easily detected. In this way, the configuration of (−)-4-methoxypentanoic acid [(−)-(VIII), obtained by partial resolution of the racemic acid] was correlated with that of (−)-lactic acid.[26,27] Although the direct conversion of (−)-(V) into (−)-(VIII) has not been reported in the literature, a configurational relationship can be established [26,28] through the sequence of correlations (VIII) ⟶ (VII), (VI) ⟶ (VII), and (VI) ⟶ (V), in each stage of which the configuration at the asymmetric centre remains unaffected. It follows from the configurational correlation of (−)-lactic acid and D(+)-glyceraldehyde [29] that the asymmetric carbon atom in (−)-pentane-1,4-diol is also related to D-glyceraldehyde. Since this asymmetric carbon atom was originally $C_{(5)}$ in desosamine, the amino-sugar may be allocated to the D-series.

Experimental

Paper electrophoresis was performed on Whatman No. 3 paper by the enclosed strip technique [30] with a borate buffer (pH 10); [31] detection was effected with ammoniacal silver nitrate (prepared from 10% silver nitate solution by addition of a small amount of 2N-sodium hydroxide and sufficient concentrated ammonia just to dissolve the resultant precipitate). Paper chromatography of acids was performed on Whatman No. 1 paper by downward irrigation with the organic phase of (1) ethyl acetate–acetic acid–water (3 : 1 : 1) or (2) isopentyl alcohol–5M-formic acid (1 : 1). For detection, chromatograms were freed from acid by air-drying and sprayed with Chlorophenol Red.[32]

Isolation of Desosamine Hydrochloride.—In a modification of the method of Flynn and his co-workers,[12] a solution of erythromycin (40 g.) in ethanol (240 ml.) was boiled under reflux with 6N-hydrochloric acid (640 ml.) for 4 hr. The solution was cooled, decanted from a tar, continuously extracted with chloroform overnight, decolorised with charcoal, and concentrated. Crystallisation of the syrupy residue from ethanol–ether (at −10°) gave desosamine hydrochloride (6·4 g.), which after recrystallisation was obtained as colourless needles, m. p. 189—190° (decomp.), $[\alpha]_D^{20}$ +50·7° (equilibrium) (*c* 2·03 in H_2O). Flynn *et al.*[12] record m. p. 183—184°.

Degradation of Desosamine with Sodium Hydroxide.—(*a*) A solution of desosamine hydrochloride (0·21 g.) in water (5 ml.) and N-sodium hydroxide (20 ml.) was stored at room temperature while evolved gases were swept into 0·05N-hydrochloric acid (100 ml.) by a current of nitrogen gas. At intervals, aliquot parts (5 ml.) of the acid solution were titrated against 0·05N-sodium hydroxide. After 3 hr., when only 15% of the theoretical quantity of dimethylamine had been evolved, the reaction temperature was raised to 50°; after a further 20 hr., 91% of the dimethylamine had been released and the reaction was terminated. The decreased alkalinity of the reaction mixture (titration of a 1 ml. aliquot part with standard acid) indicated a 65% conversion of desosamine into acidic products. The cooled solution was passed through a column of Amberlite IR-120 resin (H^+ form; 100 ml.), thereafter treated with a chloroform

[24] Levene and Haller, *J. Biol. Chem.*, 1925, **65**, 49; 1926, **67**, 329; 1926, **69**, 165, 569.
[25] Levene, Haller, and Walti, *J. Biol. Chem.*, 1927, **72**, 591.
[26] Doering and Young, *J. Amer. Chem. Soc.*, 1952, **74**, 2997.
[27] Wiberg, *J. Amer. Chem. Soc.*, 1952, **74**, 3891.
[28] Levene and Haller, *J. Biol. Chem.*, 1929, **83**, 177.
[29] Wolfrom, Lemieux, Olin, and Weisblat, *J. Amer. Chem. Soc.*, 1949, **71**, 4057.
[30] Foster, *Chem. and Ind.*, 1952, 1050.
[31] Foster, Newton-Hearn, and Stacey, *J.*, 1956, 30.
[32] Brown, *Nature*, 1951, **167**, 441.

solution of methyldi-n-octylamine (5% v/v) to remove mineral acid,[33] heated under reflux for 18 hr. with an excess of calcium carbonate, filtered, and then dried in the frozen state. The infrared spectra (KCl discs) of this product and that obtained by degradation of desosamine with lime-water were indistinguishable, and showed $\nu_{max.}$ at 1600 (CO_2^-) and 3600 cm.$^{-1}$ (free OH).

(*b*) In a similar degradation, desosamine hydrochloride (3·5 g.) was treated with N-sodium hydroxide (350 ml.) at 50° for 48 hr. After cations and hydrochloric acid had been removed, the solution was concentrated to give a colourless syrup (2·28 g.) which was examined by paper chromatography. In addition to an acidic product [compound *A*, R_F 0·75 and 0·60 in solvents (1) and (2), respectively], a second component (compound *B*) was detected with Chlorophenol Red as a bright blue spot at the solvent front with both systems. A similar mixture of degradation products (3·47 g.) was separated on a cellulose column (55 × 4·5 cm.) by using solvent (2). Chromatographically homogeneous compound *B* (1·135 g.) was eluted first, and was followed by a mixture of compounds *A* and *B*, and then homogeneous compound *A* (0·945 g.). Refractionation of the mixed products yielded additional pure compound *A* (0·23 g.). Compound *A* showed $\nu_{max.}$ (liquid film) at 1740 (δ-lactone C=O) and 3600 cm.$^{-1}$ (free OH), and was tentatively identified as the δ-lactone of 2,5-dihydroxyhexanoic acid. Compound *B* showed $\nu_{max.}$ at, *inter alia*, 1600, 1660, 1705, and 3300—3500 cm.$^{-1}$; it was not examined further.

(−)-*Hexane*-1,2,5-*triol*.—A solution of compound *A* (0·84 g.) in tetrahydrofuran (50 ml.) was added dropwise to a stirred suspension of lithium aluminium hydride (1 g.) in tetrahydrofuran (250 ml.). The mixture was heated under reflux for 4 hr., and the excess of reductant in the cooled solution was then decomposed with water. The filtered solution was concentrated (200 ml.), deionised with Amberlite IR-120 (H^+ form; 500 ml.) and Deacidite E (CO_3^{2-} form; 30 ml.), and again concentrated. Distillation of the crude product (0·55 g.), $[\alpha]_D$ −6·8° (*c* 18·3 in MeOH) gave (−)-*hexane*-1,2,5-*triol* (0·118 g.), b. p. 130—140°/0·5 mm., n_D^{20} 1·4715, $[\alpha]_D^{20}$ −10·2° (*c* 1·18 in H_2O), $[\phi]_D$ −14° (Found: C, 53·4; H, 10·5. $C_6H_{14}O_3$ requires C, 53·7; H, 10·45%), $\nu_{max.}$ (liquid film) 3600 cm.$^{-1}$ (free OH). Paper-electrophoretic examination of this material showed a single spot having the same mobility (M_G 0·20) as hexane-1,2,6-triol, but, in view of its origin, the product probably consisted of a pair of triols, epimeric at $C_{(2)}$. The product gave [19,34] a crystalline *tri*-(p-*phenylazobenzoate*), m. p. 159—169° [from benzene–light petroleum (b. p. 60—80°)] (Found: C, 71·4; H, 4·75; N, 10·9. $C_{45}H_{38}N_6O_6$ requires C, 71·2; H, 5·0; N, 11·1%). Repeated recrystallisation did not raise the m. p.; the infrared spectrum (Nujol mull) showed the absence of free OH. Hexane-1,2,6-triol gave a *tri*-(p-*phenylazobenzoate*), m. p. 144—146° (Found: C, 71·45; H, 5·2; N, 11·1. $C_{45}H_{38}N_6O_6$ requires C, 71·2; H, 5·0; N, 11·1%).

Periodate Oxidation of (−)-*Hexane*-1,2,5-*triol*.—(*a*) A solution of (−)-hexane-1,2,5-triol (0·0185 g.) in water (5 ml.) was treated with 0·25M-sodium metaperiodate (5 ml.), and the volume was rapidly adjusted to 25 ml. The consumption of oxidant was followed by the standard method,[35] and the liberated formaldehyde was determined by the chromotropic acid method.[36] The triol rapidly (6 min.) consumed 1·0 mol. of periodate with release of 1·1 mol. of formaldehyde. Under similar conditions, hexane-1,2,6-triol consumed 0·98 mol. of oxidant and released 1·0 mol. of formaldehyde.

(*b*) After storage for 1 hr., a solution of the 1,2,5-triol (0·20 g.) and sodium metaperiodate (0·35 g., 1·1 mol.) in water (25 ml.) was treated with an aqueous solution (10 ml.) containing barium chloride dihydrate (0·40 g.). Precipitated salts were removed and sodium borohydride (0·10 g.) was added to the solution which was then stored overnight. After the excess of reductant had been destroyed by addition (to pH 6) of 10% acetic acid, the solution was basified (pH 9) with sodium hydrogen carbonate and extracted with ether continuously for 2 days. The residue obtained by concentration (at atmospheric pressure) of the ether extract was dissolved in methanol and the solvent was removed at atmospheric pressure. The dissolution and evaporation were repeated. On distillation, the crude *product*, $[\alpha]_D^{20}$ −13·4° (*c* 1·05 in MeOH) gave D-(−)-pentane-1,4-diol (0·05 g.), b. p. 150—160° (bath)/12 mm. (Found: C, 57·4; H, 11·5. $C_5H_{12}O_2$ requires C, 57·7; H, 11·5%). A solution of the diol (4 mg.) in dry CCl_4 (10 ml.) had $\nu_{max.}$ at 3634 (ε 33) and 3479 cm.$^{-1}$ (ε 15) for free and intramolecularly bonded

[33] Smith and Page, *J. Soc. Chem. Ind.*, 1948, **67**, 48.
[34] Woolfolk, Beach, and McPherson, *J. Org. Chem.*, 1955, **20**, 391.
[35] Jackson, *Org. Reactions*, 1944, **2**, 341.
[36] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.

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hydroxyl groups, respectively. The intrument and method used for the measurement of this spectrum are described elsewhere.[37] The diol gave a single spot of zero mobility during paper electrophoresis in borate buffer, and readily formed a *di*-(p-*phenylazobenzoate*), m. p. 118—119·5° [from benzene–light petroleum (b. p. 60—80°)] (Found: C, 71·4; H, 5·3; N, 10·9. $C_{31}H_{28}N_4O_4$ requires C, 71·5; H, 5·4; N, 10·8%). The rotatory dispersion pattern for the diol is recorded below:

λ (mμ)	600	500	400	350	330	320	310	300	290
[φ]	−8°	−12°	−31°	−45°	−52°	−56°	−59°	−67°	−79°

(±)-*Pentane*-1,4-*diol*.—A solution of lævulic acid (5 g.) in tetrahydrofuran (20 ml.) was added dropwise to a stirred suspension of lithium aluminium hydride (5 g.) in tetrahydrofuran (100 ml.). The mixture was heated under reflux overnight and the excess of reductant was decomposed with water. After the solution had been concentrated to remove tetrahydrofuran, it was extracted with chloroform continuously for 2 days, and the extract concentrated. Distillation of the crude product (2·5 g., 55%) gave (±)-pentane-1,4-diol, b. p. 140—145° (bath)/12 mm., n_D^{21} 1·4465. The infrared spectrum (liquid film) of this diol was indistinguishable from that of (−)-pentane-1,4-diol, and showed the following absorptions (cm.$^{-1}$): 3300sb, 2900s, 1430mb, 1370m, 1330mb, 1230w, 1180w, 1130m, 1090m, 1055s, 1035s, 1010s, 995msh, 940m, 900w, 875w, 830w. The (±)-diol gave a crystalline *di*-(p-*phenylazobenzoate*), m. p. 161—162° [from benzene–light petroleum (b. p. 60—80°)] (Found: C, 71·7; H, 5·3. $C_{31}H_{28}N_4O_4$ requires C, 71·5; H, 5·4%).

The authors thank Eli Lilly and Company for generous gifts of erythromycin, and Professor W. Klyne for the optical rotatory dispersion measurements.

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EDGBASTON, BIRMINGHAM, 15. [*Received, May 17th*, 1961.]

[37] Dobinson and Foster, *J.*, 1961, 2338.

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951. *Carcinogenic Nitrogen Compounds. Part XXXI.*[1] *Benzacridines and Other Nitrogen-heterocyclic Derivatives of* m-*Ethylaniline.*

By NG PH. BUU-HOÏ, P. JACQUIGNON, and E. ALLEGRINI.

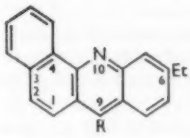
A number of substituted angular 1,2- and 3,4-benzacridines and 1,2- and 3,4-benzophenarsazines have been synthesised from *m*-ethylaniline for evaluation of carcinogenic activity, together with other nitrogen-containing heterocyclic derivatives of this amine.

INTRODUCTION of an ethyl radical into the molecule of polycyclic aromatic hydrocarbons such as 1,2-benzanthracene and similar nitrogen-bearing heterocycles such as 1,2-benzacridine, either enhances or decreases the carcinogenic activity of the basic molecule, depending on the site of the substitution. Thus, 5- and 10-ethyl-1,2-benzanthracene are considerably more active than 1,2-benzanthracene itself, whereas the 8-isomer is completely inactive;[2] in the 3,4-benzacridine series,* the 7-ethyl-9-methyl derivative is less carcinogenic than the non-ethylated substance.[3] We have already reported syntheses of 5-, 7-, and 9-ethyl derivatives of 1,2- and 3,4-benzacridine,[4] and to extend these studies 6-ethylbenzacridines have now been prepared.

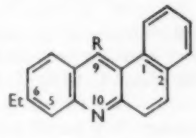
* The numbering of the benzacridines in this paper follows the recommendations of the I.U.P.A.C. which was used by us in Part XXIX (*J.*, 1961, 384), but differs from that used in some earlier papers in this series.

[1] Part XXX, Buu-Hoï and Saint-Ruf, *J.*, 1961, 2258.
[2] Cf. Shubik and Hartwell, "Compounds which have been tested for Carcinogenic Activity," National Cancer Institute, Bethesda, 1957.
[3] Cf. Lacassagne, Buu-Hoï, Daudel, and Zajdela, *Adv. Cancer Res.*, 1956, **4**, 315.
[4] Buu-Hoï and Jacquignon, *J.*, 1959, 3095.

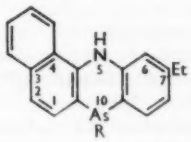
The starting material, *m*-ethylaniline, was conveniently prepared by reduction of 3-nitroacetophenone to 3-aminoacetophenone, followed by Wolff–Kishner reduction; this procedure ensures a product that is free from *ortho*- and *para*-isomers. The reaction of paraformaldehyde and *m*-ethylaniline with α- or with β-naphthol [5] yielded 6-ethyl-3,4- (I; R = H) and 1,2-benzacridine (II; R = H), respectively. 6-Ethyl-9-methyl- (I; R = Me) and 6,9-diethyl-3,4-benzacridine (I; R = Et) were prepared by a modified



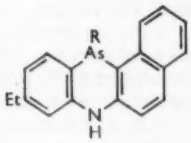
(I)



(II)



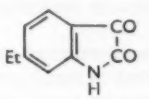
(III)



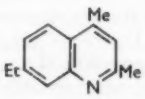
(IV)

Bernthsen reaction,[6] from *N*-*m*-ethylphenyl-1-naphthylamine with acetic and propionic anhydride, and 6,9-diethyl-1,2-benzacridine (II; R = Et) was similarly obtained from *N*-*m*-ethylphenyl-2-naphthylamine. The secondary diarylamines were prepared from *m*-ethylaniline and α- or β-naphthol; [7] their condensation with arsenic trichloride gave 10-chloro-7-ethyl-5,10-dihydro-3,4- (III; R = Cl) and -1,2-benzophenarsazine (IV; R = Cl). Replacement of the halogen by a methyl group, to give 7-ethyl-5,10-dihydro-10-methyl-3,4- (III; R = Me) and -1,2-benzophenarsazine (IV; R = Me), was achieved by means of methylmagnesium iodide.[8]

(V)



(VI)



Among the other nitrogen heterocycles prepared from *m*-ethylaniline, 6-ethylisatin (V) was obtained in low yields by a Martinet reaction involving diethyl oxomalonate; [9] it is worth mention that this cyclisation led to an apparently homogeneous product, whereas in the more usual Sandmeyer isatin synthesis as applied to *m*-substituted anilines mixtures of the two possible cyclisation products are obtained.[10] Similarly, a Combes reaction [11] with acetylacetone afforded 7-ethyl-2,4-dimethylquinoline (VI), which must have contained none (or very little) of the isomeric 5-ethyl-2,4-dimethylquinoline as the liquid base gave a sharp-melting picrate; with hexane-2,5-dione, *m*-ethylaniline furnished 1-*m*-ethylphenyl-2,5-dimethylpyrrole.

Preliminary biological tests carried out in this Institute show 6-ethyl-9-methyl-3,4-benzacridine to be appreciably carcinogenic.

Experimental

Preparation of m-*Ethylaniline.*—*m*-Nitroacetophenone, m. p. 76°, was best prepared by nitrating acetophenone (60 g.) in solution in sulphuric acid (300 g.), cooled in ethanol–solid carbon dioxide, by means of nitric acid (*d* 1·4134; 55 g.) in sulphuric acid (165 g.); reduction to *m*-aminoacetophenone, m. p. 97°, was effected by iron powder and hydrochloric acid, this procedure being more convenient than that using iron and acetic acid.[12] A solution of the

[5] For similar reactions with *m*-toluidine, see Buu-Hoï, Royer, and Hubert-Habart, *J.*, 1955, 1082.
[6] Buu-Hoï and Lecocq, *Compt. rend.*, 1944, **218**, 792; Buu-Hoï, *J.*, 1946, 792.
[7] Knoevenagel, *J. prakt. Chem.*, 1914, **89**, 1; Buu-Hoï, *J.*, 1952, 4346.
[8] Seide and Gorski, *Ber.*, 1929, **62**, 2186; Buu-Hoï, Hiong-Ki-Wei, and Royer, *Rev. Sci.*, 1944, **82**, 3237.
[9] Martinet, *Ann. Chim.* (*France*), 1919, **11**, 15.
[10] Sandmeyer, *Helv. Chim. Acta*, 1919, **2**, 234.
[11] Combes, *Compt. rend.*, 1888, **106**, 1536; Buu-Hoï and Guettier, *Rec. Trav. chim.*, 1946, **65**, 502.
[12] Rupe, Braun, and von Zembruski, *Ber.*, 1901, **34**, 3522.

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amino-ketone (15 g.) in diethylene glycol (38 g.) was refluxed with hydrazine hydrate (15 g.) and potassium hydroxide (15 g.) for 8 hr., with removal of water; after cooling and dilution with water, the product was taken up in ether, washed with water, dried (Na_2SO_4), recovered, and fractionated, giving *m*-ethylaniline (11 g., 80%), b. p. 214°/760 mm. This amine (1 g.) and tetrachlorophthalic anhydride (1 g.) in acetic acid (20 c.c.), when refluxed for 10 min., yielded *tetrachloro*-N-m-*ethylphenylphthalimide*, leaflets (from acetic acid) (1·2 g.), m. p. 192°, giving orange solutions in *NN*-dimethylaniline (Found: C, 49·1; H, 2·5. $C_{16}H_9Cl_4NO_2$ requires C, 49·4; H, 2·3%).

1-m-*Ethylphenyl*-2,5-*dimethylpyrrole*.—Hexane-2,5-dione (2 g.) and *m*-ethylaniline (2 g.) were refluxed for 1 hr. with one drop of acetic acid, and the product then distilled, giving the *pyrrole* (2·5 g.), b. p. 261—262°/755 mm., n_D^{24} 1·5586 (Found: C, 84·0; H, 8·5; N, 7·3. $C_{14}H_{17}N$ requires C, 84·4; H, 8·6; N, 7·0%).

7-*Ethyl*-2,4-*dimethylquinoline* (VI).—Acetylacetone (5 g.) and *m*-ethylaniline (6 g.) were refluxed for 5 hr., and the crude anil formed was heated for 1 hr. on the water-bath with sulphuric acid (50 c.c.). After cooling and basification with aqueous ammonia, the product was taken up in benzene, washed with water, dried (Na_2SO_4), recovered, and distilled; the oil obtained gave a *picrate*, orange needles, m. p. 210° (from ethanol) (Found: N, 13·1. $C_{19}H_{18}N_4O_7$ requires N, 13·4%). Basification with ammonia yielded the free *quinoline* (6 g.), b. p. 298°/751 mm., $n_D^{22\cdot5}$ 1·5951 (Found: C, 84·0; H, 8·5. $C_{13}H_{15}N$ requires C, 84·3; H, 8·2%).

6-*Ethylisatin* (V).—A solution of *m*-ethylaniline (10 g.) and diethyl oxomalonate (13 g.) in acetic acid (50 c.c.) was refluxed for 1 hr.; after cooling, dilute hydrochloric acid was added, the precipitate of crude ethyl dioxindole-3-carboxylate obtained was suspended in 15% aqueous potassium hydroxide (30 c.c.), and the suspension boiled until a homogeneous solution was obtained. This was left to cool, then filtered, and acidified with acetic acid. Recrystallisation of the precipitate from acetic acid afforded 6-*ethylisatin* as orange needles (1 g.), m. p. 185° (Found: C, 68·6; H, 5·5. $C_{10}H_9NO_2$ requires C, 68·6; H, 5·2%).

6-*Ethyl*-3,4-*benzacridine* (I; R = H).—To a boiling mixture of *m*-ethylaniline (10 g.) and α-naphthol (15 g.), paraformaldehyde (10 g.) was added in small portions; after the violent evolution of water had subsided, the mixture was refluxed for 1 min., then fractionated *in vacuo*. The portion of b. p. >260°/17 mm. was converted into a *picrate* which recrystallised from ethanol–benzene as orange needles (3 g.), m. p. 245° (decomp. >230°) (Found: C, 61·9; H, 3·6; N, 11·6. $C_{25}H_{18}N_4O_7$ requires C, 61·7; H, 3·7; N, 11·6%). Basification with aqueous ammonia gave the free *base*, crystallising as yellowish needles, m. p. 90°, from light petroleum (Found: C, 88·4; H, 6·0. $C_{19}H_{15}N$ requires C, 88·7; H, 5·9%).

6-*Ethyl*-1,2-*benzacridine* (II; R = H).—A similar Ullmann reaction, performed with β-naphthol, furnished an orange-red oil, b. p. 260—270°/14 mm., which was converted into a *picrate* (5 g.), crystallising as yellow needles, m. p. 225° (decomp. >205°), from xylene (Found: N, 11·3. $C_{25}H_{18}N_4O_7$ requires N, 11·6%). The free *base* crystallised from ethanol as almost colourless needles, m. p. 123° (Found: C, 88·6; H, 5·9; N, 5·5. $C_{19}H_{15}N$ requires C, 88·7; H, 5·9; N, 5·3%).

N-m-*Ethylphenyl*-1-*naphthylamine*.—A mixture of *m*-ethylaniline (15 g.), α-naphthol (20 g.), and iodine (1 g.) was refluxed for 20 hr.; after cooling, the product was taken up in benzene, washed with aqueous sodium hydroxide, then with water, dried (Na_2SO_4), recovered, and fractionated *in vacuo*. The secondary *amine* was a viscous yellow oil (17 g.), b. p. 244—245°/23 mm., n_D^{27} 1·6655 (Found: C, 87·3; H, 7·1; N, 5·8. $C_{18}H_{17}N$ requires C, 87·4; H, 6·9; N, 5·7%); the violet picrate decomposed on recrystallisation from methanol.

N-m-*Ethylphenyl*-2-*naphthylamine*.—Prepared from *m*-ethylaniline (15 g.), β-naphthol (20 g.), and iodine (1 g.) as above, this *amine*, b. p. 249—250°/17 mm., crystallised as needles (13 g.), m. p. 44°, from heptane (Found: C, 87·2; H, 7·2%); its *picrate* formed deep violet leaflets, m. p. 90°, from methanol (Found: N, 11·7. $C_{24}H_{20}N_4O_7$ requires N, 11·7%).

6-*Ethyl*-9-*methyl*-3,4-*benzacridine* (I; R = Me).—A mixture of *N*-*m*-ethylphenyl-1-naphthylamine (7 g.), acetic anhydride (7 g.), and freshly fused zinc chloride (7 g.) was refluxed for 48 hr.; after cooling, the mixture was treated with 20% aqueous sodium hydroxide, and the acridine was taken up in benzene, dried (Na_2SO_4), recovered, and distilled *in vacuo*. The portion of b. p. 280—286°/20 mm. crystallised from ethanol as yellowish needles (2 g.), m. p. 91° (Found: C, 88·5; H, 6·6; N, 5·3. $C_{20}H_{17}N$ requires C, 88·6; H, 6·3; N, 5·2%). The *picrate* formed golden-yellow needles, m. p. 234° (decomp. >190°), from toluene (Found: N, 10·9. $C_{26}H_{20}N_4O_7$ requires N, 11·2%).

6,9-*Diethyl*-3,4-*benzacridine* (I; R = Et).—Prepared as above from *N*-*m*-ethylphenyl-1-naphthylamine (6 g.), propionic anhydride (6 g.), and zinc chloride (6 g.), this *acridine*, b. p. 275—277°/16 mm., formed yellowish prisms (1·8 g.), m. p. 83°, from heptane (Found: C, 88·2; H, 6·5. $C_{21}H_{19}N$ requires C, 88·5; H, 6·7%) [*picrate*, orange-yellow prisms, m. p. 239° (decomp. >210°), from xylene (Found: N, 10·6. $C_{27}H_{22}N_4O_7$ requires N, 10·8%)].

6,9-*Diethyl*-1,2-*benzacridine* (II; R = Et).—Similarly prepared from *N*-*m*-ethylphenyl-2-naphthylamine, this *acridine*, b. p. 271—273°/15 mm., crystallised as yellowish needles, m. p. 121°, from cyclohexane (Found: C, 88·3; H, 6·3%) [*picrate*, orange-yellow prisms, m. p. 248° (decomp. >210°), from xylene (Found: N, 10·5%)].

10-*Chloro*-7-*ethyl*-5,10-*dihydro*-3,4-*benzophenarsazine* (III; R = Cl).—A solution of *N*-*m*-ethylphenyl-1-naphthylamine (2·5 g.) and arsenic trichloride (2 g.) in dry *o*-dichlorobenzene (10 c.c.) was gently refluxed for 90 min.; after cooling, the precipitate formed was collected and recrystallised from xylene, giving golden-yellow needles (2 g.) of the *phenarsazine*, m. p. 232° (decomp. >220°), whose solutions in sulphuric acid were red (Found: C, 60·5; H, 4·3. $C_{18}H_{15}AsClN$ requires C, 60·8; H, 4·2%).

10-*Chloro*-7-*ethyl*-5,10-*dihydro*-1,2-*benzophenarsazine* (IV; R = Cl), similarly prepared from *N*-*m*-ethylphenyl-2-naphthylamine, formed deep yellow prisms, m. p. 272° (decomp. >258°), from xylene (Found: C, 60·5; H, 4·5%), giving red solutions in sulphuric acid.

7-*Ethyl*-5,10-*dihydro*-10-*methyl*-3,4-*benzophenarsazine* (III; R = Me).—To a Grignard reagent (2 mol.), prepared from methyl iodide and magnesium in ether, compound (III; R = Cl) was added in small portions (1 mol.), and after the vigorous reaction had subsided, the solution was refluxed for 10 min.; after cooling and addition of ice-cold aqueous ammonium chloride, the ethereal layer was collected and dried (Na_2SO_4), the solvent removed, and the residual *phenarsazine* recrystallised from methanol, giving shiny colourless prisms (0·4 g.), m. p. 128°, whose solutions in sulphuric acid were yellow (Found: C, 67·9; H, 5·3. $C_{19}H_{18}AsN$ requires C, 68·1; H, 5·4%).

7-*Ethyl*-5,10-*dihydro*-10-*methyl*-1,2-*benzophenarsazine* (IV; R = Me), prepared from compound (IV; R = Cl), formed colourless prisms, m. p. 132°, from methanol (Found: C, 67·8; H, 5·5%).

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THE RADIUM INSTITUTE, THE UNIVERSITY OF PARIS. [*Received, May 17th*, 1961.]

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952. *Nitratopentacarbonylmanganese*(I).*

By C. C. ADDISON, M. KILNER, and A. WOJCICKI.

The preparation of nitratopentacarbonylmanganese(I), the first nitrato-metal carbonyl, is reported. The infrared and ultraviolet spectra, thermal stability, conductivity in solution, solubility properties, and some reactions of the compound are discussed. Where appropriate, comparison is made with the pentacarbonylmanganese(I) halides.

NUMEROUS derivatives of the metal carbonyls are known in which one or more of the carbonyl groups are replaced by neutral ligands such as amines and alkyl- or aryl-substituted phosphines and arsines.[1] Less abundant, but equally well characterised, are derivatives in which negative ligands such as iodide, bromide, and chloride replace carbon monoxide groups in the carbonyls with resultant oxidation of the central metal.[2] These halide ions have empty *d*-orbitals which can participate in the π-bonding to the metal and thus stabilise its low-valency state.

* For a preliminary note, see *Proc. Chem. Soc.*, 1961, 202.

[1] See, *e.g.*, the review by Hieber, *Angew. Chem.*, 1952, **64**, 465.
[2] See Anderson, *Quart. Rev.*, 1947, **1**, 331.

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In view of the respective properties of carbon monoxide and the nitrate group, the nitrato-carbonyls might be expected to display very low stability. The nitrate group is a good oxidising agent and is not normally regarded as capable of stabilising low-valency states in transition metals, particularly if the latter are combined with good reducing ligands, such as carbon monoxide. Again, if the nitrate group co-ordinates through a single oxygen atom, the latter possesses no empty orbitals which could be used for π-bonding with the metal. It is therefore not surprising that no nitrato-carbonyl has previously been prepared.

In order to investigate the possibility of preparing a nitrato-carbonyl, manganese compounds were chosen for two main reasons. First, pentacarbonylmanganese halides are stable, crystalline compounds which are almost certainly octahedral. The maximum stability of the metal carbonyl halides is attained with manganese compounds, and there was reason to believe that a manganese carbonyl nitrate would be also the most stable representative of this class of compound. Secondly, dimanganese decacarbonyl is soluble in a wide range of solvents, which enabled solvent effects to be explored.

Attempts were first made to bring about direct substitution of the nitrate group for chloride and bromide in pentacarbonylmanganese halides, by using silver and lead nitrate in ethyl alcohol. With silver nitrate, solutions decomposed rapidly, and lead nitrate gave inseparable mixtures of products. The scale of the reactions with lead nitrate was also limited by the low solubility of this salt, and this approach was found to be impracticable. Reaction of dimanganese decacarbonyl and dinitrogen tetroxide was then examined.

The conditions chosen were based on observations made in a preliminary survey of the reactions between metal carbonyls and liquid dinitrogen tetroxide, which will be summarised briefly. The rate of reaction depends greatly on the physical state of the metal carbonyl. Liquid carbonyls (nickel tetracarbonyl and iron pentacarbonyl) react violently: solid carbonyls react much more slowly, and reaction rate is a function of surface area. All reactions are strongly dependent on temperature; dimanganese decacarbonyl and dicobalt octacarbonyl react quite readily with dinitrogen tetroxide at room temperature but reaction stops almost completely at 0°. The reaction with nickel tetracarbonyl, which proceeds with explosive violence at 0°, can be moderated somewhat at lower temperature.[3] Finally, solid cyclopentadienyl-metal carbonyls react much more readily than the solid simple carbonyls; cyclopentadienyltricarbonylmanganese, the most inert and stable of these compounds, ignites readily when added to liquid dinitrogen tetroxide.[4] The ultimate products of these reactions are anhydrous metal nitrates, oxide nitrates, or their dinitrogen tetroxide addition compounds.

The rate of reaction of dimanganese decacarbonyl was sufficiently slow for isolation of intermediate products to appear possible. The reaction was readily controlled in an excess of a solvent, but the nature of the reaction was found to depend on the particular solvent used. In ethyl acetate, reaction was very slow. In nitromethane, reaction was instantaneous, but the product separating from solution contained no carbonyl groups. In light petroleum, a yellow precipitate was formed which showed strong carbonyl absorption bands in the infrared region, and it is from this product that nitratopentacarbonylmanganese(I) has been isolated.

Experimental

Dimanganese decacarbonyl was purified by sublimation at 50°/0·1 mm. Dinitrogen tetroxide was prepared as already described.[5] Light petroleum (b. p. 40—60°) was dried over phosphoric oxide and distilled. Chloroform was washed with water to remove traces of alcohol, dried ($CaCl_2$), and freshly distilled from phosphoric oxide.

Preparation of Nitratopentacarbonylmanganese(I).—Dimanganese decacarbonyl (4 g., 0·01

[3] Addison and Johnson, unpublished results.
[4] Addison and Wojcicki, unpublished results.
[5] Addison and Thompson, *J.*, 1949, S218.

mole) was dissolved in light petroleum (250 ml.), and the solution cooled to 0°. Dinitrogen tetroxide (12 g., 0·13 mole) in light petroleum (5 ml.) at 0° was then poured into the carbonyl solution in a closed system vented to air by a phosphoric oxide guard tube. On mixing, the yellow solution of the carbonyl became deep orange and after 30 sec. became cloudy and a flocculent yellow precipitate separated. The temperature was maintained at 0° for about 40 hr., after which precipitation appeared to be virtually complete. There was no apparent change in the precipitate during the course of its formation. After 40 hr. the solvent was decanted, the residue washed with light petroleum (3 × 25 ml.) to remove traces of unchanged dimanganese decacarbonyl, and dried under reduced pressure. This residue was shown (by infrared spectrum, solubility, and elementary analyses) to be a mixture of several products. To allow the less stable impurities to decompose, the powder was allowed to remain in a dry atmosphere for 3 days, during which its colour darkened to light brown. It was then extracted with successive 10 ml. portions of pure chloroform at room temperature. Light petroleum (about 20 ml.) was added to each extract, and the solutions were cooled in acetone–solid carbon dioxide. A series of precipitates was thus obtained which were examined for purity by analyses and infrared spectra. Precipitates from early extracts were mixtures of several products; later ones consisted of nitrato- and nitro-pentacarbonylmanganese(I); and finally pure nitrato-carbonyl was obtained in the last fractions. Further samples of $Mn(CO)_5NO_3$ were isolated by fractional crystallisation of the middle portions. The pure product was obtained as a bright yellow powder.

Analyses.—For manganese content the compound was dissolved in nitric acid; the solution was boiled to oxidise the metal to manganese(II), treated with sodium bismuthate to convert manganese(II) into manganese(VII), and titrated with standard ferrous solution. Nitrogen was determined by the Kjeldahl method. Carbon was determined by combustion to carbon dioxide, with vanadium(V) oxide. In view of low values often obtained with metal carbonyl derivatives, carbon analyses were confirmed by first oxidising the material vigorously in a closed system with a mixture of chromic oxide, phosphoric acid, fuming sulphuric acid, and potassium iodate, and then determining carbon dioxide by absorption [6] (Found: Mn, 21·5; N, 5·55; C, 23·3. C_5MnNO_8 requires Mn, 21·4; N, 5·5; C, 23·4%).

Magnetic Susceptibility.—Measurements were made at room temperature by the Gouy method, with finely powdered samples.

Infrared Spectra.—Routine infrared spectra were determined on a Perkin-Elmer Infracord spectrophotometer. The spectrum of the pure product was obtained by using a Unicam S.P. 100 spectrophotometer with sodium chloride windows, and Nujol and hexachlorobutadiene as mulling agents.

Molecular Weight.—This was determined cryoscopically in nitrobenzene, which had been purified by distillation and fractional crystallisations. For a $3·2 \times 10^{-2}$m-solution of the compound, a molecular weight of 254 was obtained [Calc. for $Mn(CO)_5NO_3$: *M*, 257].

Electrical Conductivities.—Conductivity of solutions was measured by using the circuit [7] and conductivity cell [8] described elsewhere. For the conductivity measurements, pentacarbonylmanganese halides were prepared by methods described in the literature.[9,10] Nitromethane was dried over calcium chloride and phosphoric oxide, refluxed under argon, and distilled from phosphoric oxide. Deionised water and spectroscopic-grade ethyl alcohol were used.

Ultraviolet Spectra.—These were determined in chloroform by means of a Unicam S.P. 500 spectrophotometer and 0·5 cm. matched fused silica cells.

Reactions of Bromopentacarbonylmanganese(I).—(a) *With silver nitrate.* This reaction was carried out on a test-tube scale. A saturated solution of silver nitrate in ethyl alcohol was added to an equimolar solution of $Mn(CO)_5Br$ in the same solvent. The mixture darkened almost instantaneously and a black precipitate was formed. No nitro- or nitrato-carbonyls were detected in solution.

(b) *With lead nitrate.* Various conditions were tried with ethyl alcohol as solvent, but results were not reproducible. Chromatographic separation, on alumina, was not successful

[6] Dunstan, personal communication.
[7] Greenwood and Worrall, *J. Inorg. Nuclear Chem.*, 1957, **3**, 357.
[8] Groeneveld and Zuur, *Rec. Trav. chim.*, 1953, **72**, 617.
[9] Brimm, Lynch, and Sesny, *J. Amer. Chem. Soc.*, 1954, **76**, 3831.
[10] Abel and Wilkinson, *J.*, 1959, 1501.

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because of low stability of the products. Infrared spectra indicated a mixture of several products but the yields were too low to attempt separation.

Other Reactions of Dimanganese Decacarbonyl with Dinitrogen Tetroxide.—(a) *In ethyl acetate.* Dimanganese decacarbonyl (0·5 g.) in ethyl acetate (40 ml.) was mixed with dinitrogen tetroxide (5 g.) in ethyl acetate (15 ml.) at room temperature. After 20 hr. the solvent and the tetroxide were removed under reduced pressure. The yellow residue was washed with light petroleum and then recrystallised from chloroform–light petroleum. Infrared spectrum showed the presence of carbonyl, nitro-, and nitrato-groups. These products were not separated, since this technique offered no advantage over the use of light petroleum.

(b) *In nitromethane.* Dinitrogen tetroxide (4 g.) in nitromethane (5 ml.) was added to dimanganese decacarbonyl (1 g.) in nitromethane (30 ml.) at room temperature. The solution became green, and vigorous evolution of gas occurred. Slow separation of a white solid began after about 2 hr.; the infrared spectrum of this solid showed no carbonyl bands.

Results and Discussion

Several products are formed in the reaction of dimanganese decacarbonyl with dinitrogen tetroxide in light petroleum. A surprising feature is the predominance of the nitrato-carbonyl, $Mn(CO)_5NO_3$, since the ionisation $N_2O_4 \longrightarrow NO^+ + NO_3^-$ is at its minimum in non-donor solvents.[11] The formation of nitrato-carbonyl may well be due to preliminary association of dimanganese decacarbonyl with the tetroxide, possibly as an addition compound, in which the tetroxide then undergoes heterolytic rather than homolytic dissociation. The general reaction scheme is:

$$Mn_2(CO)_{10} + N_2O_4 \begin{cases} \xrightarrow[\text{dissocn.}]{\text{Homolytic}} Mn(CO)_5NO_3 \\ \xrightarrow[\text{dissocn.}]{\text{Heterolytic}} Mn(CO)_5NO_3 + Mn(CO)_x(NO)_y \end{cases}$$

In view of the formation of a nitrate complex, the NO group must also be produced, either as a nitrosyl carbonyl or as nitric oxide in solution. No gas evolution was observed, and freezing the reaction mixture at frequent intervals gave no blue colour due to dinitrogen trioxide. However, the crude product gave infrared absorption bands at 1650 and 1560 cm.$^{-1}$; these are attributed [12] to a manganese nitrosyl carbonyl which is more soluble than the nitrato-carbonyl in chloroform, and is thus removed on fractional crystallisation.

There is also clear evidence for the formation of nitropentacarbonylmanganese(I). The co-ordinated NO_2 group absorbs in the infrared region at about 1430, 1315, and 825 cm.$^{-1}$.[13] Middle fractions obtained on recrystallisation of the crude product contained absorption bands at about 1410, 1315, and 825 cm.$^{-1}$. Furthermore, analyses on these fractions showed nitrogen and manganese contents intermediate between those calculated for $Mn(CO)_5NO_3$ and $Mn(CO_5)NO_2$. The crude product also showed an absorption band at 1080 cm.$^{-1}$, which may be assigned to the nitrito-group. Nitro- and nitrito-pentacarbonylmanganese(I) were also more soluble in chloroform than the nitratocarbonyl, and were removed by fractional crystallisation.

Table 1.

Frequency (cm.$^{-1}$) ...	2060s	2002s	1486s	1284s	1010s	805w
Assignment	CO stretch		NO_2 stretch asymmetric	NO_2 stretch symmetric	NO stretch	–O·NO_2 out-of-plane vibration

Infrared Spectrum.—Principal absorption bands of the final fractions, which did not change on further crystallisation, are given in Table 1.

[11] Addison and Sheldon, *J.*, 1958, 3142, and references therein.
[12] Lewis, Irving, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 32.
[13] Penland, Lane, and Quagliano, *J. Amer. Chem. Soc.*, 1956, **78**, 887.

Pentacarbonylmanganese halides show two carbonyl absorption bands,[10] consistent with their C_4v symmetry. Since the nitrate group in co-ordination compounds is almost certainly planar,[14] the C_4v symmetry is to be expected for $Mn(CO)_5NO_3$ also, and two carbonyl stretching frequencies are in fact observed. The nitrate absorption bands leave no doubt that the nitrate group is covalently bonded to manganese.[15] Ionic nitrates exhibit only one NO_2 stretching band, at 1390 cm.$^{-1}$, and this is not observed in the spectrum.

Magnetic Susceptibility.—Nitratopentacarbonylmanganese(I), like the pentacarbonyl halides, is diamagnetic. These pentacarbonyls are d^6-octahedral, or distorted octahedral, systems, and have low spin values for their magnetic moment because of high polarisability and strong π-bonding ability of the carbonyl groups.[16]

Thermal Stability.—In the solid state at room temperature the compound is stable for several weeks. Pentacarbonylmanganese halides differ considerably from the nitrate in their volatility and thermal stability at higher temperatures. The chloride, bromide, and iodide, can be sublimed in a vacuum, and at 120° give univalent dimeric compounds of the type $[Mn(CO_4)X]_2$,[10] which on further heating decompose to their respective manganese(II) halides. The +1 oxidation state of manganese is less stable in the carbonyl nitrate than in the carbonyl halides. Heating at 55°/0·01 mm. causes disproportionation, and gives sublimed $Mn_2(CO)_{10}$ and a residue containing $Mn(NO_3)_2$ and some oxides of manganese. No $Mn(CO)_5NO_3$ was obtained in the sublimate, even on further heating. This disproportionation may be represented as:

$$4Mn(CO)_5NO_3 \longrightarrow Mn_2(CO)_{10} + 2Mn(NO_3)_2 + 10CO$$

When the compound is heated, carbon monoxide is first evolved; then dimanganese decacarbonyl sublimes and eventually dinitrogen tetroxide is evolved by decomposition of the nitrate. The two factors probably responsible for a lower stability of the nitrate are an increased ionic character of the molecule and a weaker overall π-bonding. The nitrate group is a weak ligand when co-ordinated through only one oxygen; some ionic character in the $Mn{-}O{\cdot}NO_2$ bond will render the metal positive and hence decrease the flow of its electrons to the carbonyl groups, *via* π-bonding. The overall effect will be a weakening of the Mn–CO bonds, as compared with the pentacarbonyl halides.

Solution Properties.—Increased ionic character of the compound $Mn(CO)_5NO_3$, as compared with the carbonyl halides, becomes apparent from the study of its solution properties. Conductivity measurements on fresh solutions of the nitrato-carbonyl in several solvents, and on solutions of the carbonyl halides in nitromethane, are compared in Table 2. The following points are noteworthy: (1) Each of the compounds is essentially a non-electrolyte in all of these solvents. The molar conductivities for uni-univalent

TABLE 2.

Molar conductivities.

Solute	Solvent	Temp.	Molar concn. ($\times 10^4$)	Molar conductivity μ (ohm^{-1} cm.^{2})	Age of solutions (min.)
$Mn(CO)_5NO_3$	$MeNO_2$	25°	71	0·48	3
	$MeNO_2$	0	70	0·098	3
	$MeNO_2$	24	40	<0·1	3
	EtOH	24	16	4·1	3
	H_2O	0	2	10·1	5
$Mn(CO)_5Cl$	$MeNO_2$	24	86	0·023	3
$Mn(CO)_5Br$	$MeNO_2$	23	93	0·007	3
$Mn(CO)_5I$	$MeNO_2$	24	114	0·004	3

[14] Maxwell and Mosley, *J. Chem. Phys.*, 1940, **8**, 738.
[15] Addison and Gatehouse, *J.*, 1960, 613.
[16] Chatt, *J. Inorg. Nuclear Chem.*, 1958, **8**, 515.

electrolytes in nitromethane and nitrobenzene are of the order of 90 [17] and 25 ohm^{-1} cm.^{2},[18] respectively. The nitrate is an extremely weak electrolyte even in water.[19] (2) Molar conductivities in nitromethane increase in the order $Mn(CO)_5I < Mn(CO)_5Br < Mn(CO)_5Cl < Mn(CO)_5NO_3$. This order is consistent with polarizabilities of the negative groups, leading to differences in the ionic character of the Mn–X bonds. It is also similar to the trend observed for molar conductivities of pentacarbonylrhenium halides in acetone.[10] (3) The conductivities of solutions of the pentacarbonylmanganese compounds increase with time. The changes observed are illustrated for the nitrate and chloride in Table 3. The change in conductivity of the nitromethane solutions of the nitrate is

TABLE 3.

Variation in molar conductivity (ohm^{-1} cm.^{2}) with age of solution.

			Age of solution (min.)				
Solute	Solvent	Temp.	3	5	15	30	60
$Mn(CO)_5NO_3$	$MeNO_2$	24°	0·48	0·77	2·3	4·4	7·2
$Mn(CO)_5NO_3$	$MeNO_2$	0	0·098	0·10	0·15	0·21	0·35
$Mn(CO)_5NO_3$	H_2O	0	—	10·1	13·8	26·2	34·5
$Mn(CO)_5Cl$	$MeNO_2$	23	0·023	0·098	0·40	0·70	1·3

arrested at lower temperatures and is then less than the change observed with the chloride. Aqueous solutions of the nitrate change very rapidly; measurements could not be made within the first five minutes because of slow rate of solution, but extrapolation of the values in Table 3 indicates that the nitrate first dissolves in water as a non-electrolyte.

This phenomenon can be explained on the basis of solvent replacement:

$$Mn(CO)_5NO_3 + \text{Solvent} \rightleftharpoons Mn(CO)_5\text{Solvent}^+NO_3^-$$

The formation of ionic species accounts initially for the conductivity of these solutions. The cation is unstable and on storage evolution of carbon monoxide from solution can be observed. The resulting decomposition products will no doubt be electrolytes, which contribute further to the increase in conductivity.

The molar conductivity values in non-aqueous solvents given in Table 2 are so low as to imply a negligible dissociation so far as the molecular weight of the solvent in fresh solutions is concerned, and the cryoscopic study of the nitrato-carbonyl in nitrobenzene confirms that the compound is monomeric and essentially undissociated in this medium.

The more polar nature of the $Mn–NO_3$ bond than of the M–Cl bond in these complexes is reflected in the solubility properties of the nitrato-carbonyl. It is readily soluble in alcohol, acetone, ethyl acetate, nitrobenzene, nitromethane, and chloroform; sparingly soluble in water, ether, methyl cyanide, benzene, and carbon tetrachloride; and insoluble in aliphatic hydrocarbons and carbon disulphide. Its solubility in water, although not large, is unusual since there are very few non-salt-like metal carbonyls which dissolve in water. Nitratopentacarbonylmanganese(I) in solution is much less stable than the carbonyl halides. Nevertheless, treatment of fresh aqueous solutions of the nitrato-complex does not lead to immediate oxidation of manganese(I) to manganese(II), and manganese(II) hydroxide is formed only slowly on heating.

Ultraviolet Absorption Spectra.—These were recorded for chloroform solutions in the region 280—420 mμ, and are summarised in Table 4. Dimanganese decacarbonyl, which absorbs much more strongly than the pentacarbonyl compounds, is given for comparison. Its ε value is much higher than that reported for dicobalt octacarbonyl, for which $\lambda_{max.} = 352$ mμ and $\varepsilon = 315 \pm 100$.[20] Iron pentacarbonyl [21] and nickel tetracarbonyl,[22] on the

[17] Harris and Nyholm, *J.*, 1956, 4375.
[18] Parish, Thesis, University of London, 1958.
[19] Nyholm, *J.*, 1950, 2071.
[20] Cable, Nyholm, and Sheline, *J. Amer. Chem. Soc.*, 1954, **76**, 3373.
[21] Sheline, *J. Amer. Chem. Soc.*, 1951, **73**, 1615.
[22] Thompson and Garratt, *J.*, 1934, 524.

other hand, show no absorption peaks in this region. It is significant that $\lambda_{max.}$ and ε values for the pentacarbonylmanganese(I) compounds fall into the order found for molar conductivities.

TABLE 4.

Ultraviolet absorption spectra.

	Concn. (M)	ε	$\lambda_{max.}$ (mμ)	$\lambda_{min.}$ (mμ)
$Mn_2(CO)_{10}$	0·0001	20,000	344	299
$Mn(CO)_5NO_3$	0·001	1,200	375	331
$Mn(CO)_5Cl$	0·002	620	377	339
$Mn(CO)_5Br$	0·002	420	386·5	346·5
$Mn(CO)_5I$	0·001	390	404	373

Chemical Reactions.—Nitratopentacarbonylmanganese(I) with an excess of liquid dinitrogen tetroxide gives the addition compound $Mn(NO_3)_2,N_2O_4$. Since the same product is obtained from the reaction of dimanganese decacarbonyl with an excess of the tetroxide, the nitrato-carbonyl is probably an intermediate in the latter reaction.

Preliminary studies have been made on the reaction of $Mn(CO)_5NO_3$ with pyridine. The product has been shown by infrared spectroscopy to contain pyridine, nitrate, and carbonyl groups, and may be analogous to the products obtained by Abel and Wilkinson [10] from the pentacarbonyl halides.

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THE UNIVERSITY, NOTTINGHAM. [*Received, June 8th,* 1961.]

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953. *Purines, Pyrimidines, and Imidazoles. Part XVI.*[1] *Some 1-Aminoimidazoles and Derived 9-Aminopurines.*

By R. N. NAYLOR, G. SHAW, D. V. WILSON, and (in part) D. N. BUTLER.

Hydrazine, phenylhydrazine, 1,1-dimethylhydrazine, and 2-methylsemicarbazide with ethyl *N*-(carbamoylcyanomethyl)formimidate, acetimidate, or benzimidate, and ethyl *N*-(cyano-*N*-methylcarbamoylmethyl)acetimidate gave 1-aminoimidazole-4-carboxyamides (or -*N*-methylcarboxyamides), which may be cyclised to 9-aminopurines and 9-amino-2-azapurines. 1,5-Diaminoimidazole was similarly obtained from hydrazine and ethyl *N*-(cyanomethyl)formimidate.

PART XIII [2] of this series recorded the preparation of the linear imidates (I; R = H or Me) and (II; R = H, R′ = Me, and *vice versa*) and their reactions with ammonia and primary amines to give 5-aminoimidazoles and 5-aminoimidazole-4-carboxyamides (or -*N*-methylcarboxyamides), which may be cyclised to purine derivatives by conventional methods.

Similar reaction of the imidates (I) and (II) with hydrazines could lead to 1-aminoimidazoles or the analogous 1,2,4-triazines. Completion of a pyrimidine or triazine (with nitrous acid) ring in these compounds would yield, from the imidazoles, derivatives of 9-aminopurine, and, from the triazines, derivatives of a triazinopyrimidine or triazinotriazine; the last compounds may be regarded as " dihydroazapteridines." These groups

[1] Part XV, Dewar and Shaw, *J.*, 1961, 3254. Previously " glyoxalines " was used in the series title in place of " imidazoles."

[2] Shaw, Warrener, Butler, and Ralph, *J.*, 1959, 1648.

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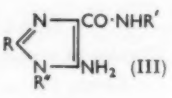
of compounds are of interest as possible growth inhibitors, and a few such compounds have been prepared recently by cyclisation of some hydrazinopyrimidines.[3]

(I) $R{\cdot}C(OEt){:}N{\cdot}CH_2{\cdot}CN$

(II) $R{\cdot}C(OEt){:}N{\cdot}CH(CN){\cdot}CO{\cdot}NHR'$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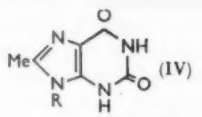
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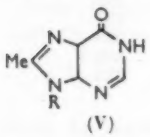
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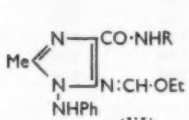
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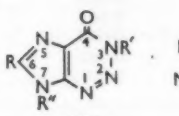
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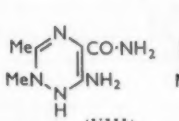
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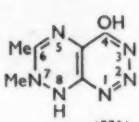
(IX)

Reaction of the imidate (II; R = Me, R′ = H) with hydrazine gave the crystalline 1-aminoimidazole (III; R = Me, R′ = H, R″ = NH_2). The structure of this compound was confirmed as follows: (1) Infrared spectra showed the absence of cyanide bands. (2) The compound could be diazotised and coupled with an alkaline solution of β-naphthol to give a red dye. (3) The compound gave a diazotisable benzylidene derivative (III; R = Me, R′ = H, R″ = N:CHPh). (4) Fusion of the compound with urea gave 9-amino-8-methylxanthine (IV; R = NH_2) which was deaminated by nitrous acid to the known 8-methylxanthine[4] (IV; R = H). (5) The imidazole with formic acid and acetic anhydride gave a diformyl derivative, and with ethyl orthoformate and acetic anhydride gave the ethoxymethylene derivative (V; R = N:CH·OEt); hydrolysis of this with hydrochloric acid afforded 9-amino-8-methylhypoxanthine (V; R = NH_2) which with nitrous acid gave 8-methylhypoxanthine (V; R = H). The last compound was also formed directly from the ethoxymethylene derivative (V; R = N:CH·OEt) and nitrous acid.

In a similar manner several other 1-aminoimidazoles have been prepared from the imidates (II; R = H, Me, or Ph, R′ = H or Me) by reaction with hydrazine, phenylhydrazine, 1,1-dimethylhydrazine and 2-methylsemicarbazide in water or alcohol. The parent 1,5-diaminoimidazole was also similarly prepared by reaction of hydrazine with ethyl *N*-(cyanomethyl)formimidate (I; R = H), being isolated as a picrate. The imidazole structure of this compound is assumed by analogy with that of the carboxyamides.

The imidazoles (III; R = Me, R′ = H or Me, R″ = Ph·NH), when heated with ethyl orthoformate, gave ethoxymethylene derivatives (VI; R = H or Me) (cf. Part XIV[5]). The derivative (VI; R = H) with acetic anhydride then gave the hypoxanthine (V; R = NHPh). Several 9-amino-2-azapurines (VII; R = H, Me, or Ph, R′ = H or Me, R″ = NH_2, NMe_2, NHPh, or NMe·CO·NH_2) have also been prepared from the corresponding aminoimidazolecarboxyamides and nitrous acid.

Reaction of the imidate (II; R = Me, R′ = H) with methylhydrazine readily gave a crystalline diazotisable amine which may be formulated as either the imidazole (III; R = Me, R′ = H, R″ = NHMe) or the 1,2,4-triazine (VIII), and in view of the well-known enhanced reactivity of the secondary amino-group in methylhydrazine, the latter structure is preferred. This compound with nitrous acid readily gave the triazinotriazine (IX) which may be regarded as a " dihydrodiazapteridine."

Experimental

1,5-Diaminoimidazole.—A solution of ethyl *N*-(cyanomethyl)formimidate[2] (0·71 g.) in methanol (5 ml.) was heated on a water bath with hydrazine hydrate (0·32 ml.) for 5 min.

[3] Pfleiderer, *Annalen*, 1958, **615**, 42; Montgomery and Temple, *J. Amer. Chem. Soc.*, 1960, **82**, 4592.

[4] Traube, *Ber.*, 1900, **33**, 1382.

[5] Shaw and Butler, *J.*, 1959, 4040.

The cooled solution with saturated methanolic picric acid (5 ml.) gave a crystalline precipitate which was collected and washed with ethanol and ether. The *imidazole picrate* (0·97 g.) recrystallised from water as yellow plates m. p. 150° (decomp.) (Found: C, 33·0; H, 2·5; N, 30·0. $C_9H_9N_7O_7$ requires C, 32·9; H, 2·8; N, 29·3%).

Ethyl N-(Carbamoylcyanomethyl)benzimidate.—When a suspension of ethyl benzimidate hydrochloride (17·5 g.) and α-amino-α-cyanoacetamide (5 g.) in water (10 ml.) was shaken for 20 min. with warming, a clear solution was obtained. This was cooled, giving a crystalline precipitate. The *benzimidate* (7·6 g.) recrystallised from ethyl acetate as plates, m. p. 109—110° (Found: C, 62·45; H, 5·5; N, 17·95. $C_{12}H_{13}N_3O_2$ requires C, 62·3; H, 5·65; N, 18·15%).

Preparation of 1,5-Diaminoimidazole-4-carboxyamides.—The imidazoles could all be diazotised and coupled with an alkaline solution of β-naphthol to give red or magenta dyes.

1,5-Diaminoimidazole-4-carboxyamide. A mixture of ethyl *N*-(carbamoylcyanomethyl)-formimidate [2] (0·35 g.) and hydrazine hydrate (0·12 ml.) in ethanol (1 ml.) was heated on a water bath for 5 min., then cooled to give a crystalline precipitate. The *imidazole* separated from methanol as needles, m. p. 222—224° (decomp.) (Found: C, 34·25; H, 5·1; N, 50·3. $C_4H_7N_5O$ requires C, 34·05; H, 5·0; N, 49·65%), $\lambda_{max.}$ 270 mμ (ε 12,100) in H_2O, and 241 (ε 8000) and 270 mμ (ε 11,400) in N/20-HCl.

5-Amino-1-anilinoimidazole-4-carboxyamide. A solution of phenylhydrazine (0·27 g.) and the last formimidate (0·35 g.) in ethanol was heated on a water bath for 5 min. The *imidazole* (0·06 g.) separated from the cooled solution and recrystallised from ethanol as needles, m. p. 245—247° (decomp.) (Found: C, 55·1; H, 5·25; N, 32·55. $C_{10}H_{11}N_5O$ requires C, 55·3; H, 5·1; N, 32·25%).

1,5-Diamino-2-methylimidazole-4-carboxyamide. Ethyl *N*-(carbamoylcyanomethyl)acetimidate [2] (0·85 g.), ethanol (2 ml.), and hydrazine hydrate (0·25 ml.) were warmed together for 5 min. and a crystalline precipitate was collected and washed with ethanol and ether. The *imidazole* (0·53 g.) separated from ethanol as needles, m. p. 270° (decomp.) (Found: C, 38·9; H, 5·7; N, 45·15. $C_5H_9N_5O$ requires C, 38·7; H, 5·85; N, 45·15%), $\lambda_{max.}$ 270 mμ (ε 13,800) in H_2O. An alcoholic solution of the base with dry hydrogen chloride gave the *hydrochloride* which separated from ethanol as needles, m. p. 240—242° (Found: C, 31·4; H, 4·65; N, 36·8. $C_5H_9N_5O,HCl$ requires C, 31·3; H, 4·7; N, 36·6%).

5-Amino-1-benzylideneamino-2-methylimidazole-4-carboxyamide. A solution of the last-mentioned base (1 g.) and benzaldehyde (0·7 g.) in ethanol (250 ml.) was boiled under reflux for 2 hr. Evaporation of the solution then gave the *benzylidene derivative* (1·1 g.) which separated from ethanol as pale yellow prisms, m. p. 246—249° (Found: C, 59·25; H, 5·25; N, 28·45. $C_{12}H_{13}N_5O$ requires C, 59·1; H, 5·35; N, 28·8%).

5-Amino-1-anilino-2-methylimidazole-4-carboxyamide. The last-mentioned acetimidate (0·85 g.), ethanol (2 ml.), and phenylhydrazine (0·54 g.) were warmed together, a vigorous exothermic reaction soon occurring. The cooled red solution gave a crystalline precipitate which was washed with ethanol and ether. The *imidazole* (0·63 g.) separated from ethanol as needles, m. p. 300° (decomp.) (Found: C, 57·4; H, 5·55; N, 30·0. $C_{11}H_{13}N_5O$ requires C, 57·15; H, 5·65; N, 30·3%), $\lambda_{max.}$ 231 (ε 16,000) and 271 mμ (ε 16,800) in EtOH.

5-Amino-1-dimethylamino-2-methylimidazole-4-carboxyamide. A suspension of the foregoing acetimidate (1·7 g.) in ethanol (4 ml.) was warmed with 1,1-dimethylhydrazine (0·63 ml.) to give a clear pale yellow solution. This was boiled for a few min., then cooled to precipitate the *imidazole* (0·96 g.) which recrystallised from ethanol as prisms, m. p. 211° (decomp.) (Found: C, 45·9; H, 7·05; N, 37·7. $C_7H_{13}N_5O$ requires C, 45·9; H, 7·1; N, 38·25%).

1,5-Diamino-2-methylimidazole-4-N-methylcarboxyamide. A solution containing ethyl *N*-(cyano-*N*-methylcarbamoylmethyl)acetimidate [2] (0·5 g.) and hydrazine hydrate (0·15 ml.) in ethanol was boiled under reflux for 30 min. The solvent was removed *in vacuo*, to give a syrup which crystallised when stirred with ether. The *imidazole* (0·36 g.) separated from ethyl acetate or methanol as needles, m. p. 182° (Found: C, 42·85; H, 6·4; N, 41·15. $C_6H_{11}N_5O$ requires C, 42·6; H, 6·55; N, 41·4%).

5-Amino-1-anilino-2-methylimidazole-4-N-methylcarboxyamide. A solution of the foregoing acetimidate (0·5 g.) in ethanol (3 ml.) was heated on a water bath for 15 min. with phenylhydrazine (0·3 ml.). The cooled solution precipitated the *imidazole* (0·28 g.) which separated from aqueous ethanol as needles, m. p. 272° (Found: C, 55·9; H, 6·2; N, 27·4. $C_{12}H_{15}N_5O,\frac{1}{2}H_2O$ requires C, 55·75; H, 6·4; N, 27·1%). A further quantity (0·41 g.) of the base was obtained from the mother liquors.

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1,5-*Diamino-2-phenylimidazole-4-carboxyamide*. A solution containing hydrazine hydrate (1·1 g.) and ethyl *N*-(carbamoylcyanomethyl)benzimidate (5 g.) in ethanol (250 ml.) was boiled under reflux for 4 hr. After 5 min. a small quantity (0·32 g.) of orange crystals had separated; these were collected. The *substance* was insoluble in water, hydrochloric acid, sodium hydroxide solution, and common organic solvents, and failed to melt below 380° (Found: C, 61·9; H, 4·1; N, 24·75. $C_{20}H_{15}N_7O_2$ requires C, 62·4; H, 3·9; N, 25·2%). The ethanolic solution was evaporated *in vacuo* to a low volume and saturated with hydrogen chloride to precipitate a solid. The *imidazole hydrochloride* (4·2 g.) separated from aqueous ethanol as needles, m. p. 210° (Found: C, 47·5; H, 4·6; N, 27·6. $C_{10}H_{11}N_5O$,HCl requires C, 47·5; H, 4·75; N, 27·6%).

5-*Amino*-1-*anilino*-2-*phenylimidazole*-4-*carboxyamide*. A mixture of phenylhydrazine (2·34 g.) and the foregoing benzimidate (5 g.) in ethanol 250 ml. was boiled under reflux for 4 hr. The solution was evaporated to a small volume and cooled to precipitate the *imidazole* (5·3 g.) which recrystallised from ethanol as needles, m. p. 234—235° (Found: C, 65·4; H, 4·95; N, 23·75. $C_{16}H_{15}N_5O$ requires C, 65·5; H, 5·15; N, 23·9%), $\lambda_{max.}$ 231 (ε 17,200) and 271 mμ (ε 15,000) in EtOH.

5-*Amino*-1-(*N-carbamoyl-N-methylamino*)-2-*methylimidazole*-4-*carboxyamide*. A suspension of ethyl *N*-(carbamoylcyanomethyl)acetimidate (1·74 g.) and 2-methylsemicarbazide [6] (0·94 g.) in dry ethanol (3·5 ml.) was shaken for 30 min. at room temperature, then heated on a water bath for 15 min. The cooled solution precipitated the *imidazole* (0·88 g.) which recrystallised from ethanol as prisms, m. p. 164° (decomp.) (Found: C, 36·25; H, 6·35; N, 36·4. $C_7H_{13}N_6O,H_2O$ requires C, 36·5; H, 6·1; N, 36·5%). A further quantity (0·18 g.) was recovered from the mother liquors.

9-*Amino*-8-*methylxanthine*.—A finely ground mixture of 1,5-diamino-2-methylimidazole-4-carboxyamide (2 g.) and urea (2 g.) was heated at 185° (bath) for 2 hr.; ammonia was evolved. The dark melt was cooled to about 40° and dissolved in hot N-sodium hydroxide (15 ml.). The filtered solution, when cooled, gave a crystalline precipitate. The *sodium salt* of 9-amino-8-methylxanthine (0·95 g.) separated from water as a *monohydrate*, m. p. >360° (Found: C, 32·6; H, 4·05; N, 32·0. $C_6H_6N_5NaO_2,H_2O$ requires C, 32·6; H, 3·6; N, 31·7%). The salt (0·95 g.) in hot water was acidified with acetic acid to precipitate 9-*amino*-8-*methylxanthine* (0·7 g.) which was obtained as needles by dissolution in sodium hydroxide solution and precipitation with acetic acid; it had m. p. >350° (Found: C, 39·6; H, 3·85; N, 36·65. $C_6H_7N_5O_2$ requires C, 39·8; H, 3·9; N, 38·65%), $\lambda_{max.}$ 237 (ε 9100) and 266 mμ (ε 11,150) in H_2O.

8-*Methylxanthine*.—Sodium nitrite (0·2 g.) was added portionwise to a stirred cold solution of 9-amino-8-methylxanthine (0·5 g.) in water (20 ml.) and N-hydrochloric acid (3 ml.). The solution was evaporated to dryness *in vacuo* and the residue extracted with ethanol. Evaporation of the extract gave 8-methylxanthine (0·25 g.) which separated from aqueous ethanol as needles, m. p. >360° (Found: C, 42·95; H, 3·55; N, 33·4. Calc. for $C_6H_6N_4O_2$: C, 43·35; H, 3·65; N, 33·75%), $\lambda_{max.}$ 283—284 mμ (ε 6600) in 0·05N-NaOH. The compound was identical with a sample prepared from 5,6-diamino-2,4-dihydroxypyrimidine and acetamide.[4]

9-*Amino*-8-*methylhypoxanthine*.—A solution of 1,5-diamino-2-methylimidazole-4-carboxyamide (3 g.) in ethyl orthoformate (20 ml.) and acetic anhydride (20 ml.) was boiled under reflux for 2 hr., then evaporated *in vacuo* to a solid from which traces of solvent were removed by evaporation with ethanol *in vacuo*. The solid, 9-*ethoxymethyleneamino*-8-*methylhypoxanthine* (2·4 g.) separated from ethanol as needles, m. p. 260—262° (Found: C, 48·65; H, 4·7; N, 31·45. $C_9H_{11}N_5O_2$ requires C, 48·85; H, 5·0; N, 31·65%). A solution of the compound (2 g.) in N-hydrochloric acid (20 ml.) was boiled under reflux for 1 hr. Evaporation then gave 9-*amino*-8-*methylhypoxanthine* (1·5 g.) which separated from aqueous ethanol as needles, m. p. 335° (decomp.) (Found: C, 43·5; H, 4·3; N, 42·2. $C_6H_7N_5O$ requires C, 43·65; H, 4·25; N, 42·4%), $\lambda_{max.}$ 252 mμ (ε 10,800) in H_2O.

8-*Methylhypoxanthine*.—9-Amino-8-methylhypoxanthine (1 g.) in water (10 ml.) and N-hydrochloric acid (6 ml.) with sodium nitrite (0·4 g.) gave a solid precipitate. 8-Methylhypoxanthine (0·7 g.) crystallised from aqueous ethanol as needles, m. p. >360° (Found: C, 47·9; H, 3·9; N, 37·15. Calc. for $C_6H_6N_4O$: C, 48·0; H, 4·05; N, 37·3%), $\lambda_{max.}$ 247 mμ (ε 12,500) in H_2O. The same compound was obtained by the reaction of nitrous acid with 9-ethoxymethyleneamino-8-methylhypoxanthine.

1,5-*Diformamido*-2-*methylimidazole*-4-*carboxyamide*.—1,5-Diamino-2-methylimidazole-4-carboxyamide (3 g.) in formic acid (20 ml.) and acetic anhydride (20 ml.) was boiled under

[6] von Brunig, *Annalen*, 1889, **253**, 11.

reflux for 2 hr. Evaporation *in vacuo* gave the *imidazole* (2·9 g.) which separated from ethanol as needles, m. p. >360° (Found: C, 40·25; H, 3·95; N, 33·45. $C_7H_9N_5O_3$ requires C, 39·8; H, 4·3; N, 33·2%).

9-*Anilino*-8-*methylhypoxanthine*.—(*a*) A mixture of 5-amino-1-anilino-2-methylimidazole-4-carboxyamide (3 g.) in ethyl orthoformate (20 ml.) and acetic anhydride (20 ml.) was boiled under reflux for 1 hr., then evaporated *in vacuo* to a solid. The *hypoxanthine* (2·6 g.) separated from ethanol as needles, m. p. >360° (Found: C, 59·6; H, 4·6; N, 29·2. $C_{12}H_{11}N_5O$ requires C, 59·7; H, 4·45; N, 29·0%). (*b*) The foregoing imidazole (2 g.) was boiled under reflux with ethyl orthoformate (20 ml.) for 1 hr.; evaporation *in vacuo* gave 1-*anilino*-5-*ethoxymethyleneamino*-2-*methylimidazole*-4-*carboxyamide* (1·6 g.) which separated from ethanol as needles, m. p. >360° (Found: C, 58·55; H, 5·4; N, 24·45. $C_{14}H_{17}N_5O_2$ requires C, 58·5; H, 5·95; N, 24·2%). This compound gave the hypoxanthine described under (*a*) when heated with acetic anhydride.

1-*Anilino*-5-*ethoxymethyleneamino*-2-*methylimidazole*-4-*N*-*methylcarboxyamide*.—5-Amino-1-anilino-2-methylimidazole-4-*N*-methylcarboxyamide (0·25 g.) was boiled under reflux with ethyl orthoformate (5 ml.) for 30 min., then evaporated *in vacuo* to a gum which solidified when rubbed with ether. The *product* (0·07 g.) crystallised from aqueous ethanol as needles, m. p. 131—132° (Found: C, 59·75; H, 6·05; N, 23·15. $C_{15}H_{19}N_5O_2$ requires C, 59·8; H, 6·35; N, 23·25%).

7-*Amino*-4-*hydroxy*-6-*methyl*-7H-*imidazo*[4,5-d]-v-*triazine*.—A solution of 1,5-diamino-2-methylimidazole-4-carboxyamide (1 g.) in 2N-hydrochloric acid (3·25 ml.) and water (12 ml. was added slowly to one of sodium nitrite (0·45 g.) in water (10 ml.) with cooling. Dark-brown crystals were soon obtained. The *imidazotriazine* (0·87 g.) separated from aqueous acetic acid as dark brown plates, m. p. >360° (Found: C, 36·15; H, 3·35; N, 50·25. $C_5H_6N_6O$ requires C, 36·15; H, 3·65; N, 50·6%).

7-*Anilino*-4-*hydroxy*-6-*methyl*-7H-*imidazo*[4,5-d]-v-*triazine*.—To a cold solution of 5-amino-1-anilino-2-methylimidazole-4-carboxyamide (0·55 g.) in N-hydrochloric acid (2·4 ml.) and water (12 ml.) was added dropwise sodium nitrite (0·164 g.) in water (3 ml.), giving a yellow precipitate. The *imidazotriazine* (0·33 g.) separated from ethanol as pale yellow plates, m. p. 190° (decomp.) (Found: C, 54·6; H, 4·0; N, 34·45. $C_{11}H_{10}N_6O$ requires C, 54·55; H, 4·15; N, 34·7%).

7-*Dimethylamino*-4-*hydroxy*-6-*methyl*-7H-*imidazo*[4,5-d]-v-*triazine*.—A solution of 5-amino-1-dimethylamino-2-methylimidazole-4-carboxyamide (0·44 g.) in N-hydrochloric acid (6 ml.) and water (4 ml.) was added to sodium nitrite (0·2 g.) in water (2 ml.) during 10 min. with cooling. The solution was set aside overnight, then evaporated *in vacuo* to a small volume; crystals separated. The *triazine* (0·1 g.) recrystallised from water as prisms, m. p. 161° (decomp.) (Found: C, 43·35; H, 5·15; N, 43·75. $C_7H_{10}N_6O$ requires C, 43·3; H, 5·2; N, 43·3%).

7-*Amino*-3,4-*dihydro*-3,6-*dimethyl*-4-*oxo*-7H-*imidazo*[4,5-d]-v-*triazine*.—1,5-Diamino-2-methylimidazole-4-*N*-methylcarboxyamide (0·105 g.) in 10N-hydrochloric acid (0·065 ml.) and water (2 ml.) with sodium nitrite (0·045 g.) in water (1 ml.) gave a yellow precipitate. The *imidazotriazine* (0·1 g.) crystallised from aqueous ethanol as pale yellow needles, m. p. 139° (Found: C, 39·95; H, 4·3; N, 45·5. $C_6H_8N_6O$ requires C, 40·0; H, 4·5; N, 46·65%).

7-*Anilino*-3,4-*dihydro*-3,6-*dimethyl*-4-*oxo*-7H-*imidazo*[4,5-d]-v-*triazine*.—5-Amino-1-anilino-2-methylimidazole-4-*N*-methylcarboxyamide (0·29 g.) in 10N-hydrochloric acid (0·2 ml.) and water (5 ml.) was slowly added to sodium nitrite (0·082 g.) in water (2 ml.) to precipitate the *imidazotriazine* (0·25 g.) which separated from aqueous ethanol as pale yellow needles, m. p. 108—109° (Found: C, 55·6; H, 4·45; N, 31·8. $C_{12}H_{12}N_6O$ requires C, 56·25; H, 4·7 N, 32·8%).

6-*Amino*-2,3-*dimethyl*-1,2,4-*triazine*-5-*carboxyamide* (?).—A suspension of ethyl *N*-(carbamoylcyanomethyl)acetimidate (4·25 g.) in a solution of methylhydrazine sulphate (4 g.) in N-sodium hydroxide (11·1 ml.) and water (2 ml.) was shaken and gently warmed to give a clear solution which when cooled gave a crystalline precipitate. The *triazine* (1·43 g.) recrystallised from water as diamond-shaped plates, m. p. 254° (decomp.) (Found: C, 42·5; H, 6·55; N, 41·4. $C_6H_{11}N_5O$ requires C, 42·6; H, 6·5; N, 41·4%), $\lambda_{max.}$ 271 mμ (ε 13,500). The triazine was diazotised and coupled with an alkaline solution of β-naphthol to give an intense magenta colour.

4-*Hydroxy*-6,7-*dimethyl*-[1,2,4]-*triazino*[6,5-d]-v-*triazine* (?).—The foregoing triazine (0·34 g.) in N-hydrochloric acid (2 ml.) and water (5 ml.) was slowly added to a solution of sodium nitrite (0·14 g.) in water (1 ml.) with cooling. A yellow precipitate appeared after 5 min., was

collected after 45 min., and was washed with water, ethanol, and ether. The *triazine* (0·32 g.) formed pale yellow prisms, m. p. 194° (decomp.) (Found: C, 40·05; H, 4·75; N, 46·3. $C_6H_8N_6O$ requires C, 40·0; H, 4·45; N, 46·65%).

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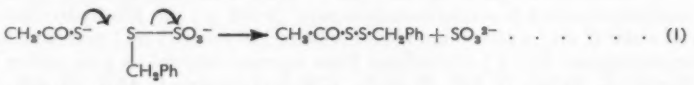
954. *New Syntheses of Trisulphides.*

By BRIAN MILLIGAN, B. SAVILLE, and J. M. SWAN.

Trisulphides are obtained conveniently by the reaction of sodium alkyl thiolsulphates with sodium sulphide; the new method is illustrated by preparation of diethyl, diallyl, dibenzyl, diphenacyl, di-*p*-tolyl and di-(2-methylpent-2-enyl) trisulphide. Sodium benzyl thiolsulphate also yields dibenzyl trisulphide on reaction with thiolacetate in alkaline solution; in neutral solution is obtained the intermediate acetyl benzyl disulphide which yields the trisulphide on further reaction with sodium benzyl thiolsulphate and also on reaction with sulphide. Attempts to extend these new trisulphide syntheses were not always successful, the disulphide rather than the trisulphide being obtained.

TRISULPHIDES are generally prepared by reaction of the corresponding thiols with sulphur dichloride in inert solvents, but this method is not readily applicable to complex water-soluble thiols. The method is also limited in the case of unsaturated trisulphides owing to possible side reactions of olefinic groups with sulphur dichloride. Thus, although attempts to prepare the trisulphide analogue of cystine, di-(2-amino-2-carboxyethyl) trisulphide, by several new methods now described have been unsuccessful, a number of other trisulphides were obtained in good yields under attractively mild conditions.

The essential discovery of these new synthetical methods resulted from an attempt to prepare acetyl benzyl disulphide through the action of sodium thiolacetate on sodium benzyl thiolsulphate according to an elementary substitution of the kind:



$$CH_3{\cdot}CO{\cdot}S^- + S(CH_2Ph){\cdot}SO_3^- \longrightarrow CH_3{\cdot}CO{\cdot}S{\cdot}S{\cdot}CH_2Ph + SO_3^{2-} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Finding the product of the above experiment to be dibenzyl trisulphide led us to suppose that the intermediate acetyl benzyl disulphide had rapidly undergone hydrolysis (cf. Böhme and Zinner [1]) to benzyl hydrogen disulphide which reacted with another molecule of sodium benzyl thiolsulphate as follows:

$$CH_3{\cdot}CO{\cdot}S{\cdot}S{\cdot}CH_2Ph + OH^- \longrightarrow CH_3{\cdot}CO_2H + Ph{\cdot}CH_2{\cdot}S{\cdot}S^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$Ph{\cdot}CH_2{\cdot}S{\cdot}S^- + Ph{\cdot}CH_2{\cdot}S{\cdot}SO_3^- \longrightarrow Ph{\cdot}CH_2{\cdot}S{\cdot}S{\cdot}S{\cdot}CH_2Ph + SO_3^{2-} \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The formation of acetyl benzyl disulphide, as required by the above reaction sequence, was proved by allowing benzyl thiolsulphate to react with sodium thiolacetate in an aqueous buffer at pH 7·0 or in the presence of Ba^{2+} at pH 8·5. Under these conditions the chief product was indeed acetyl benzyl disulphide, which if further heated in suspension at 50° (as an emulsion) in a buffer at pH 8·5 gave some dibenzyl trisulphide. This points to an alternative trisulphide-forming reaction:

$$Ph{\cdot}CH_2{\cdot}S{\cdot}S^- + Ph{\cdot}CH_2{\cdot}S{\cdot}S{\cdot}CO{\cdot}CH_3 \longrightarrow Ph{\cdot}CH_2{\cdot}S{\cdot}S{\cdot}S{\cdot}CH_2Ph + CH_3{\cdot}CO{\cdot}S^- \quad . \quad . \quad . \quad (4)$$

[1] Böhme and Zinner, *Annalen*, 1954, **585**, 142.

although the yield of trisulphide was much higher when sodium benzyl thiolsulphate was included with the intermediate acetyl benzyl disulphide. Heating acetyl benzyl disulphide in ethanol with cyclohexylamine as base gave *N*-cyclohexylacetamide, but no trisulphide could be isolated even when sodium benzyl thiosulphate was included in the mixture. The reason for this remains obscure.

Treatment of pyridinium *p*-tolyl thiolsulphate with sodium thiolacetate also afforded di-*p*-tolyl trisulphide, but sodium *o*-nitrophenyl thiolsulphate gave only di-*o*-nitrophenyl disulphide under a wide range of conditions. The presumed intermediate, acetyl *o*-nitrophenyl disulphide, obtained authentically by an independent method, likewise gave only di-*o*-nitrophenyl disulphide under conditions expected to yield trisulphide. Two explanations can be advanced: either the initially formed trisulphide is decomposed according to reactions (5) and (6) (cf. Minoura [2])

$$SO_3^{2-} + RS{\cdot}S{\cdot}SR \longrightarrow RS{\cdot}S{\cdot}SO_3^- + RS^- \quad (5)$$

$$RS^- + RS{\cdot}S{\cdot}SO_3^- \longrightarrow RS{\cdot}SR + {}^-S{\cdot}SO_3^- \quad (6)$$

or owing to parity in leaving-group propensities of thiolacetate and *o*-nitrobenzyl sulphide ($Ar{\cdot}CH_2{\cdot}S{\cdot}$) the following reactions become important:

$$CH_3{\cdot}CO{\cdot}S^- + CH_3{\cdot}CO{\cdot}S{\cdot}SR \longrightarrow CH_3{\cdot}CO{\cdot}S{\cdot}S{\cdot}CO{\cdot}CH_3 + RS^- \quad (7)$$

$$RS^- + CH_3{\cdot}CO{\cdot}S{\cdot}SR \longrightarrow RS{\cdot}SR + CH_3{\cdot}CO{\cdot}S^- \quad (8)$$

Since our postulated mechanism for the successful production of trisulphides (reactions 1—3) is essentially dependent upon the intermediate existence of monoionised disulphide entities ($RS{\cdot}S^-$) it was evident that the latter would also result from the action of sulphide ion on sodium alkyl thiolsulphates which might finally yield trisulphides according to reactions (9) and (10):

$$S^{2-} + S(R)\text{—}SO_3^- \longrightarrow {}^-S\text{—}S(R) + SO_3^{2-} \quad (9)$$

$$RS{\cdot}S^- + RS{\cdot}SO_3^- \longrightarrow RS{\cdot}S{\cdot}SR + SO_3^{2-} \quad (10)$$

Experiments with benzyl, phenacyl, and *p*-tolyl thiolsulphates gave the corresponding trisulphides in good yield. Similarly, aqueous solutions of thiolsulphates prepared *in situ* from sodium thiosulphate and alk(en)yl halides (R = Et, allyl, or 2-methylpent-2-enyl) gave good yields of very pure trisulphides on treatment with sodium sulphide. However, reaction of sodium *N*-cyclohexylcarbamoylmethyl thiolsulphate, sodium phenoxycarbonylmethyl thiolsulphate, sodium *o*-nitrophenyl thiolsulphate, or the sodium salt of *S*-sulphocysteine (sodium 2-amino-2-carboxyethyl thiolsulphate) with sulphide ion gave only the corresponding disulphides.

Experimental

Light petroleum refers to the fraction of b. p. 55—70° uness stated otherwise.

Thiolsulphates.—Sodium benzyl thiolsulphate,[3] sodium phenacyl thiolsulphate,[4,5] sodium *N*-cyclohexylcarbamoylmethyl thiolsulphate,[6] sodium phenoxycarbonylmethyl thiolsulphate,[5] sodium *o*-nitrophenyl thiolsulphate,[7] and the sodium salt of *S*-sulphocysteine [8] were prepared by reported methods.

Pyridinium p-*Tolyl Thiolsulphate.*—*N*-Sulphopyridinium (kindly provided by Allied Chemical Corp., N.Y., U.S.A.) (1·66 g.) and toluene-*p*-thiol (1·29 g.) were heated together

[2] Minoura, *J. Soc. Rubber Ind. Japan*, 1950, **23**, 213; *Chem. Abstr.*, 1953, **47**, 7247.
[3] Purgotti, *Gazzetta*, 1890, **20**, 25.
[4] Baker and Barkenbus, *J. Amer. Chem. Soc.*, 1936, **58**, 262.
[5] Milligan and Swan, *J.*, 1961, 1194.
[6] Milligan and Swan, *J.*, 1959, 2969.
[7] Lecher and Hardy, *J. Org. Chem.*, 1955, **20**, 475.
[8] Sorbo, *Acta Chem. Scand.*, 1958, **12**, 1990.

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on a steam bath for 15 min. according to the general method of Baumgarten.[9] Crystallisation of the resulting slurry from ethanol yielded the *product* (1·3 g., 44%) as plates, m. p. 128°. After several recrystallisations from methanol–ether the m. p. had fallen to 120° (Found: C, 50·7; H, 4·7; N, 4·9; S, 22·5. $C_{12}H_{13}NO_3S_2$ requires C, 50·9; H, 4·6; N, 4·9; S, 22·6%).

Reaction of Thiolsulphates with Thiolacetate.—(i) A solution of sodium benzyl thiolsulphate (4·5 g.) in water (20 ml.) and a solution (pH 8·5) of thiolacetic acid (0·77 g.) and tri(hydroxymethylamino)methane (2·5 g.) in water (30 ml.) were shaken together for 1·5 hr. The product (1·26 g.), isolated by extraction with ethyl acetate, crystallised from light petroleum, giving dibenzyl trisulphide (0·95 g., 34%), m. p. 49° (lit.,[10] 49°) (Found: C, 60·4; H, 5·3; S, 34·8. Calc. for $C_{14}H_{14}S_3$: C, 60·4; H, 5·0; S, 34·6%). When the reaction was carried out at pH 12, the yield was 65%.

(ii) A solution of thiolacetic acid (3·1 g.), tri(hydroxymethylamino)methane (10 g.), and barium acetate monohydrate (22 g.) in water (80 ml.) was adjusted to pH 8·5. To this solution was added a solution of sodium benzyl thiolsulphate (18 g.) in water (80 ml.) which caused the slow formation of an inorganic precipitate. The mixture was left overnight and the product was isolated by extraction with ethyl acetate. Crystallisation from light petroleum gave acetyl benzyl disulphide (5·7 g., 36%), m. p. 56—57° (lit.,[1] 58—59°) (Found: C, 55·1; H, 5·3; S, 32·1. Calc. for $C_9H_{10}OS_2$: C, 54·5; H, 5·1; S, 32·3%). Dibenzyl trisulphide was present in the mother liquors. Reaction at 50° gave mainly dibenzyl trisulphide.

(iii) Thiolacetic acid (1·3 g.) was shaken with a solution of sodium benzyl thiolsulphate (3·7 g.) in phosphate buffer (30 ml.; pH 7) for 1 hr., a crude product (1·46 g.) being precipitated. Crystallisation of this from light petroleum gave acetyl benzyl disulphide (1·1 g., 34%), m. p. 56—57°. However, when this experiment was repeated, mixtures of acetyl benzyl disulphide and dibenzyl trisulphide were obtained.

(iv) Pyridinium *p*-tolyl thiolsulphate (3·6 g.) was added to a solution of barium acetate monohydrate (3·4 g.), tri(hydroxymethylamino)methane (3·0 g.), and thiolacetic acid (0·5 g.) in water (40 ml.) at pH 9·2. After 3 hr. the pH had fallen to 6·8. The resulting precipitate was filtered off, dried, and extracted with ethyl acetate. Evaporation of the extract gave an oil (1·4 g.), which was chromatographed in light petroleum on alumina. Elution with this solvent gave a crystals (0·86 g.), m. p. 78° after crystallisation from methanol. The m. p. was undepressed on admixture with di-*p*-tolyl trisulphide, prepared by reaction of toluene-*p*-thiol with sulphur dichloride.[12]

Reactions of Acetyl Benzyl Disulphide.—(i) Acetyl benzyl disulphide (0·48 g.) was added to a solution of sodium benzyl thiolsulphate (0·54 g.) and tri(hydroxymethylamino)methane (5 g.) in water (30 ml.), adjusted to pH 8·5. One drop of a non-ionic detergent was added, and the mixture was shaken at 50° for 10 min. and then at room temperature for 2 hr. The product (0·36 g.), isolated by extraction with ethyl acetate, gave dibenzyl trisulphide (0·24 g., 36%), m. p. 48—49°, on crystallisation from light petroleum. Addition of an excess of sodium sulphite to the reaction mixture had no effect and a similar yield of trisulphide was obtained from an experiment at pH 12. When sodium benzyl thiolsulphate was omitted, the acetyl benzyl disulphide was recovered largely unchanged; a few hand-picked crystals were identified as dibenzyl trisulphide.

(ii) Tri(hydroxymethylamino)methane (5 g.) was dissolved in 0·1M-sodium sulphide (25 ml.) and the pH was adjusted to 8·5. Acetyl benzyl disulphide (1·0 g.) was added and the mixture was shaken at 50° for 30 min. and then set aside overnight. Extraction with ethyl acetate gave a product (0·78 g.), from which dibenzyl trisulphide (0·57 g., 78%), m. p. 49°, was obtained by crystallisation from light petroleum.

(iii) Acetyl benzyl disulphide (0·30 g.) and cyclohexylamine (0·2 g.) were heated under reflux in ethanol (10 ml.) for 15 min., and the mixture was then evaporated. The residue was partitioned between ethyl acetate and dilute hydrochloric acid. Evaporation of the ethyl acetate extract gave a residue (0·27 g.) from which *N*-cyclohexylacetamide, m. p. 104°, was obtained by crystallisation from light petroleum.

Acetyl o-Nitrophenyl Disulphide.—Thiolacetic acid (4 g.) in water (20 ml.) was titrated to pH 7 with 10N-sodium hydroxide, and the solution made into a slurry with *o*-nitrobenzenesulphenyl chloride (5·5 g.). After 5 min. the mixture was filtered and the precipitate

[9] Baumgarten, *Ber.*, 1930, **63**, 1331.
[10] Smythe and Forster, *J.*, 1910, **97**, 1195.

fractionally crystallised from ethanol. *Acetyl o-nitrophenyl disulphide* (3·1 g., 46%) was obtained as yellow prisms, m. p. 77°, substantially free from di-*o*-nitrophenyl disulphide (Found: N, 5·7; S, 27·0. $C_8H_7NO_3S_2$ requires N, 6·1; S, 28·0%).

Reaction of Thiolsulphates with Sodium Sulphide.—0·1M-Sodium sulphide (100 ml.) was added to sodium benzyl thiolsulphate (4·5 g.) in M-phosphate buffer (50 ml.; pH 8·0) and, after 1 hr., the resulting precipitate of dibenzyl trisulphide (1·8 g., 65%) was filtered off and crystallised from ethanol (m. p. and mixed m. p. 49°). Likewise, sodium phenacyl thiolsulphate gave diphenacyl trisulphide (37%), m. p. 78° (lit.,[11] 85—86°) (Found: C, 57·1; H, 4·3; S, 29·3. Calc. for $C_{16}H_{14}O_2S_3$: C, 57·5; H, 4·2; S, 28·8%); and pyridinium *p*-tolyl thiolsulphate gave di-*p*-tolyl trisulphide, isolated by ethyl acetate extraction and recrystallisation from methanol, having m. p. and mixed m. p. 81° (lit.,[12] 76—77°). Similar reactions of sodium *N*-cyclohexylcarbamoylmethyl thiolsulphate, sodium phenoxycarbonylmethyl thiolsulphate, and sodium *o*-nitrophenyl thiolsulphate gave only the corresponding disulphides in yields of 76, 14, and 74%, respectively.

Preparation of Trisulphides from Unisolated Thiolsulphates.—A mixture of sodium thiosulphate pentahydrate (0·25 mole) and the appropriate alkyl or alkenyl halide (0·2 mole) in 60% v/v ethanol–water (100 ml.) was heated under reflux until the mixture was homogeneous, indicating substantially complete formation of the intermediate thiolsulphate. The mixture was then distilled at reduced pressure to remove most of the ethanol, cooled, extracted with light petroleum (b. p. 30—40°), and treated with sodium sulphide (0·09 mole) in water (200 ml.). The crude trisulphide, deposited as an oil, was then extracted with light petroleum, washed with water, and dried. Removal of solvent gave a residue further purified by vacuum distillation. Yields of 65—70% were obtained.

In this way allyl chloride gave diallyl trisulphide, b. p. 66—67°/0·8 × 10^{-3} mm., n_D^{20} 1·5896, shown to be 99% pure by gas–liquid chromatography (Found: C, 40·4; H, 5·6; S, 53·9. Calc. for $C_6H_{10}S_3$: C, 40·4; H, 5·6; S, 53·9%), together with a little fore-fraction, b. p. 60—95°/12 mm. Similarly, ethyl bromide gave diethyl trisulphide, b. p. 79·8—80·0°/11 mm., n_D^{20} 1·5657 (Found: C, 31·1; H, 6·4; S, 62·2. Calc. for $C_4H_{10}S_3$: C, 31·2; H, 6·5; S, 62·3%) (98—99% pure by gas–liquid chromatography), together with a small fraction (*ca.* 8% of total distillate) having b. p. 55—77°/11 mm. and containing some diethyl disulphide. The amount of this impurity was markedly reduced when the aqueous solution of the intermediate thiolsulphate was covered with a layer of light petroleum before addition of sodium sulphide. The procedure was designed to minimise disulphide formation by preventing reaction between sulphite and trisulphide (cf. reactions 9, 10, 5, and 6). This procedure applied in the case of 1-chloro-2-methylpent-2-ene (synthesis to be described later) gave the very involatile di-(2-methylpent-2-enyl) trisulphide which without further treatment was found by a combination of chemical and gas–liquid chromatographic analyses to be about 97·5% pure.

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[11] Bloch and Bergmann, *Ber.*, 1920, **53**, 968.
[12] Troeger and Hornung, *J. prakt. Chem.*, 1899, **60**, 134.

955. *The Di-π-cyclopentadienyl Hydrides of Tantalum, Molybdenum, and Tungsten.*

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The di-π-cyclopentadienyl hydrides of tantalum, molybdenum, and tungsten have been prepared. High-resolution nuclear magnetic resonance spectra of these compounds and of the trihydride cations of molybdenum and tungsten have been measured. For the trihydride species of tantalum and tungsten the patterns of the high-field lines show that there are two equivalent hydrogen atoms in an A_2B grouping. This observation is discussed with reference to the base character and structure of di-π-cyclopentadienylmetal hydrides.

In a previous note [1] infrared and high-resolution nuclear magnetic resonance spectra of di-π-cyclopentadienylrhenium hydride were reported; it was also shown that the compound behaves as a base and can be protonated to give the cation $(\pi\text{-}C_5H_5)_2ReH_2^+$. Analogous di-π-cyclopentadienyl hydrides of molybdenum, tungsten,[2,3] and tantalum [4] have been briefly described and we here present further details of our work together with a discussion of the structure of this series of complexes on the basis of evidence gained principally from high-resolution nuclear magnetic resonance spectra.

Preparations and Chemical Properties.—The hydride complexes are prepared in high yields by the interaction of the anhydrous metal chlorides ($MoCl_5$, WCl_6, or $TaCl_5$) with a solution of sodium cyclopentadienide in tetrahydrofuran containing an excess of sodium borohydride. Without addition of borohydride to the sodium cyclopentadienide solution only low yields of the hydrides can be obtained since the hydride ion required must come from the solvent or from traces of excess of cyclopentadiene or cyclopentene present in the reaction mixture.

The tantalum hydride, $(\pi\text{-}C_5H_5)_2TaH_3$, is a white crystalline compound which is very sensitive to air; the molybdenum and tungsten hydrides, $(\pi\text{-}C_5H_5)_2MH_2$, form yellow crystals, the former being more sensitive to air than the latter, which can be handled briefly in air. The tantalum compound is sparingly soluble in light petroleum but it is moderately soluble in benzene; the other hydrides are soluble in light petroleum as well as in other common solvents. Solutions of all three compounds decompose rapidly when exposed to air. The compounds are soluble in halogenated solvents and in carbon disulphide but react with them quite rapidly, the order of reactivity being Ta > Mo > W; dichloromethane reacts much more slowly than carbon tetrachloride.

Like $(\pi\text{-}C_5H_5)_2ReH$, the molybdenum and tungsten compounds behave as bases and are soluble in dilute aqueous acids [3] and in trifluoroacetic acid, to give the ions $(\pi\text{-}C_5H_5)_2MH_3^+$; with gaseous hydrogen chloride or bromide the white deliquescent halide salts are formed. The tantalum hydride does not appear to behave as a base, even in trifluoroacetic acid, and is decomposed by aqueous acids.

Spectroscopic Studies.—The most significant information bearing on the structure of these hydrides comes from high-resolution nuclear magnetic resonance studies. The data are presented in the Table, and the high-field region for $(\pi\text{-}C_5H_5)_2TaH_3$ and $(\pi\text{-}C_5H_5)_2WH_3^+$ is shown in Fig. 1. The spectra of all of the species are similar to those of $(\pi\text{-}C_5H_5)_2ReH$ and $(\pi\text{-}C_5H_5)_2ReH_2^+$ and also to those of the ferrocenonium ion, $(\pi\text{-}C_5H_5)_2FeH^+$, and its ruthenium and osmium analogues which were reported [5] (during the course of our work) to be formed when the neutral molecules $(\pi\text{-}C_5H_5)_2M$ are dissolved in boron trifluoride

[1] Green, Pratt, and Wilkinson, *J.*, 1958, 3916.
[2] Green, Street, and Wilkinson, *Z. Naturforsch.*, 1959, **14**b, 738.
[3] Fischer and Hristidu, *Z. Naturforsch.*, 1960, **15**b, 135.
[4] McCleverty and Wilkinson, *Chem. and Ind.*, 1961, 288.
[5] Curphey, Santer, Rosenblum, and Richards, *J. Amer. Chem. Soc.*, 1960, **82**, 5249.

hydrate. In all these cases there are two main groups of resonance lines, one at low and one at high fields relative to tetramethylsilane. The low-field line of relative intensity 10

High-resolution proton magnetic resonance spectra (at 56·45 Mc./sec.).

	Hydride line			π-C_5H_5 line	
		Splitting (cycles/sec.)			
Compound	τ	by other hydride protons	by π-C_5H_5	τ	Splitting (cycles/sec.) by hydride protons
$(\pi\text{-}C_5H_5)_2TaH_3$ [a] ...	11·63 (B) } 13·02 (A_2) }	9·6 [d]		5·24	
$(\pi\text{-}C_5H_5)_2MoH_2$ [a] ...	18·76	—	Not resolved Line width 1·6 cycles/sec.	5·64 (triplet)	0·96
$(\pi\text{-}C_5H_5)_2MoH_3^+$ [b] ...	16·08	—	Not resolved Line width 1·4 cycles/sec.	4·38	
$(\pi\text{-}C_5H_5)_2WH_2$ [a] ...	22·28 [e] (" septuplet ")	—	0·7$_5$	5·76 (triplet)	0·7$_5$
$(\pi\text{-}C_5H_5)_2WH_3^+$ [c] ...	16·08 (B) } 16·44 (A_2) }	8·5	Not resolved Line widths $\leqslant$2·1 cycle/sec.	4·39	Not resolved Line width 1·4 cycle/sec.

[a] In benzene. [b] In trifluoroacetic acid. [c] In concentrated hydrochloric acid, reference $Me_3C{\cdot}OH$, for which $\tau = 8{\cdot}69$. [d] Calculated by using data tabulated by Corio (*Chem. Rev.*, 1960, **60**, 363). [e] The hydride lines of the tungsten compounds show weak satellite doublets from those molecules containing the isotope ^{183}W with spin $\frac{1}{2}$ (abundance 14·3%). The tungsten-proton splitting is 36·6 cycles/sec. for the dihydride and 47·8 cycles/sec. for the A_2 protons in the trihydride cation.

is due to the ten equivalent protons of the π-C_5H_5 groups. The bands from molybdenum and tungsten dihydride show fine structure due to electron-coupled spin–spin interaction with the hydrogen atoms bound to the metal; this splitting is of the same order, *ca.*

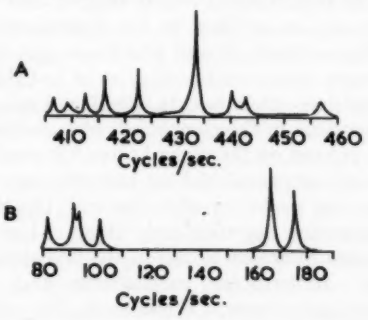

FIG. 1. High-resolution nuclear magnetic resonance spectrum in the high-field region of (A) $(\pi\text{-}C_5H_5)_2WH_3^+$ and (B) $(\pi\text{-}C_5H_5)_2TaH_3$.

1 cycle/sec., as that in $(\pi\text{-}C_5H_5)_2ReH$ and $(\pi\text{-}C_5H_5)_2FeH^+$. The high-field lines occur in the region characteristic for hydrogen atoms bound to transition-metal atoms and the areas, relative to the low-field lines, taken as 10, confirm the stoicheiometries of the various species.

For the dihydride species of rhenium, molybdenum, and tungsten, there is only one high-field proton resonance line, as in $(\pi\text{-}C_5H_5)_2ReH$ and the ferrocenonium ion. For the rhenium and tungsten compounds, the fine structure on these lines is due to coupling with the π-C_5H_5 ring protons although all the expected components (eleven) cannot be resolved. It thus appears that the two hydrogen atoms in $(\pi\text{-}C_5H_5)_2MH_2$ are in equivalent environments. This is not true, however, of the three hydrogen atoms in $(\pi\text{-}C_5H_5)_2TaH_3$ and $(\pi\text{-}C_5H_5)_2WH_3^+$ since in these cases the high-field line patterns (Fig. 1) are characteristic of A_2B groupings [6] with two equivalent protons and one non-equivalent one. The cation

[6] See Jackman, " Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, London, 1959.

$(\pi\text{-}C_5H_5)_2MoH_3^+$ in water or in trifluoroacetic acid shows only a single line of relative intensity 3, which suggests that in this case there is a slow exchange with the protons of the solvent; this exchange also occurs in benzene–trifluoroacetic acid mixtures. A solution of $(\pi\text{-}C_5H_5)_2WH_2$ in D_2O—DCl mixtures shows no high field line, again indicating a slow exchange with the solvent which is complete within a few minutes. In neither the molybdenum or tungsten case is the exchange rate fast enough to make the solvent and hydridic proton lines coalesce.

The infrared spectra of the neutral hydrides have been measured down to 750 cm.$^{-1}$, and measurements below 750 cm.$^{-1}$ are given elsewhere.[7] The metal-to-hydrogen bond stretching frequencies occur in the region around 2000 cm.$^{-1}$; the band in $(\pi\text{-}C_5H_5)_2TaH_3$ is exceptionally intense, presumably owing to the greater ionic character in the metal-to-hydrogen bond. Even under the highest available resolution on a grating instrument only one symmetrical band is found for the M–H absorption in molybdenum and tungsten dihydrides, but for $(\pi\text{-}C_5H_5)_2TaH_3$ this band has weak shoulders.

Discussion.—We have discussed previously [1] the high-resolution nuclear magnetic resonance spectra of $(\pi\text{-}C_5H_5)_2ReH(D)$ and $(\pi\text{-}C_5H_5)_2ReH_2(D_2)^+$ and have shown that the structure with the hydrogen atom(s) lying between the metal atom and the $\pi\text{-}C_5H_5$ rings which had been proposed [8] for these compounds (and which has recently been suggested [5] as a possibility for the ferrocenonium ion) is unlikely. The main unsettled question in this work was whether the metal-to-ring axes are linear, as in ferrocene, or are angular. This problem has also been considered by others [7] in the light of dipole moment and far-infrared data on the rhenium, molybdenum, and tungsten species. Our present observations of the non-equivalence of the hydrogen atoms bound to the metal in the tantalum and tungsten trihydrides, and the ability of the neutral di-π-cyclopentadienyls or hydrides of Mo, W, Re, Fe, Ru, and Os to take up a proton, suggest a structural interpretation of the properties of this class of compounds.

The experimental results suggest that in the complexes $(\pi\text{-}C_5H_5)_2MH_x$ ($x = 1$, 2, or 3) there are, in addition to the hybrid orbitals involved in metal-to-ring bonding, three bonding orbitals, two of which are equivalent. These three orbitals can be occupied by hydrogen atoms exclusively, as in $(\pi\text{-}C_5H_5)_2TaH_3$, or by hydrogen atoms and lone pairs of electrons—thus $(\pi\text{-}C_5H_5)_2ReH$ will have two lone pairs. In view of the steric effects of lone pairs in the compounds of transition and non-transition elements which have lone pairs present on the central atom,[9] it would be remarkable if the lone pairs in the present series of compounds did not have the same steric consequences and occupy bond positions. Hence we could consider the $(\pi\text{-}C_5H_5)_2MH_x$ species as 5-co-ordinate, probably with a configuration approximately trigonal bipyramidal, in which case the non-equivalence of the three hydrogen atoms in the trihydrides implies that the metal-to-ring axes are non-linear. In ferrocene, ruthenocene, and, presumably, osmocene, the metal-to-ring axes are certainly linear. While sterically active lone pairs are therefore presumably absent, there must nevertheless be primarily non-bonding (*versus* the rings) electrons on the metal atom. The addition of a proton to such a linear di-π-cyclopentadienyl compound would be expected to distort the rings as in the above cases. The greatly reduced basicity (protonation of ferrocene occurs in BF_3,H_2O,[5] but we find no high-field line in trifluoroacetic or concentrated sulphuric acid), compared with, say, $(\pi\text{-}C_5H_5)_2ReH$, is consistent with involvement of the non-bonding electrons in subsidiary metal-to-ring bonding. We have so far found no evidence in any case for the uptake of more than one proton, but it is only to be expected on electrostatic grounds that the second base constant would be very small. Even in BF_3,H_2O the ratio of the low and high field lines for the rhenium compound is 10 : 2.

[7] Fritz, Hristidu, Hummel, and Schneider, *Z. Naturforsch.*, 1959, **15**b, 419.
[8] Liehr, *Naturwiss.*, 1957, **44**, 61.
[9] See Gillespie and Nyholm, *Quart. Rev.*, 1957, **11**, 339; "Progress in Stereochemistry," Butterworths, London, 1958, Vol. II; Nyholm, *op. cit.*, Vol. I, 1954.

In extending these ideas, it now seems likely that all di-π-cyclopentadienyl metal compounds of the general type $(\pi\text{-}C_5H_5)_2MX_n$ will have non-linear metal-to-ring axes. Non-linearity has indeed been confirmed for $(\pi\text{-}C_5H_5)_2TiCl_2Al(C_2H_5)_2$.[10] It also follows that some compounds such as $(\pi\text{-}C_5H_5)_2TiX_2$ should have a vacant orbital, and again there is evidence that this is so from the existence [11] of $[(\pi\text{-}C_5H_5)_2TiPh_2]^-$.

The above qualitative views of the nature of the hydride species have received mathematical support within the framework of molecular-orbital theory. Ballhausen and Dahl [12] have shown that the metal-to-π-C_5H_5-ring bonding, as made evident by orbital overlaps, is very little reduced even if the metal-to-ring axes are at angles down to 135°; even further distortion can doubtless occur with a sacrifice in metal to ring bonding energy. Further, with angular bonds, it follows immediately that there will remain on the metal atom three strongly space-directed orbitals (cf. Fig. 2): ψ_0 (an sp hybrid), ψ_{-y}, and ψ_y ($spd_{x^2-y^2}$,d_{z^2} hybrids), two of which are equivalent (ψ_{-y}, ψ_y), of precisely the character required. When ferrocene is protonated distortion to the angular form will occur with the hydrogen atom probably located in ψ_0, so that the electron pairs in the other two orbitals could take part in subsidiary metal-to-ring bonding. In $(\pi\text{-}C_5H_5)_2ReH$ the proton could be similarly

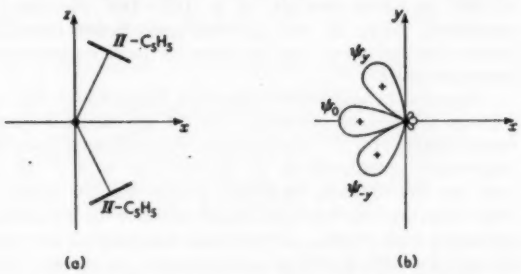

FIG. 2. Diagram showing disposition of $(\pi\text{-}C_5H_5)$ rings and non-bonding orbitals in $(\pi\text{-}C_5H_5)_2MH_n$ compounds.

located, but in $(\pi\text{-}C_5H_5)_2ReH_2^+$ the nuclear magnetic resonance spectra show equivalence of the protons, as is the case for the molybdenum and tungsten dihydrides, so that presumably ψ_{-y} and ψ_y are now occupied.

The dipole-moment [7] and infrared data are consistent with non-linearity of the metal-to-ring axes, but provide little conclusive evidence either for or against them. Thus it might have been expected (cf. ref. 1) that, if the H–M–H bonds in the dihydride species are at an angle, both the symmetric and the asymmetric stretching modes would have been evident in the infrared region. This is not so. However, it is not necessarily surprising, since with the very heavy central metal atoms, together with the fact that if the H–M–H angle is about 90° as the molecular-orbital picture suggests, the coupling could be very small. A similar case occurs for the dialkyl- and aryl-tin dihydrides, where the H–Sn–H group is certainly angular, in which only one Sn–H stretching frequency can be observed.[13] It is also possible, in principle, to decide on structures with parallel or twisted rings in $(\pi\text{-}C_5H_5)_2M$ compounds by infrared studies, as discussed, for example, for dicyclopentadienyl-tin and -lead.[14,15] For the species $(\pi\text{-}C_5H_5)_2ReH$, $(\pi\text{-}C_5H_5)_2Mo(W)H_2$, and $(\pi\text{-}C_5H_5)_2Mo(W)H_3^+$ there are indeed differences in the number of bands observed [7] in the 400—600 cm.$^{-1}$ region associated with metal-to-ring stretching frequencies. However, only three or four of the predicted 7—9 bands appear. Further, the measurements were made in mulls where crystal lattice effects provide unknown and often large variables, so that such small differences among weak bands cannot be taken as providing substantial

[10] Natta, Corradini, and Bassi, *J. Amer. Chem. Soc.*, 1955, **77**, 3604.
[11] Summers, Uloth, and Holmes, *J. Amer. Chem. Soc.*, 1955, **77**, 3604.
[12] Ballhausen and Dahl, *Acta Chem. Scand.*, in the press.
[13] Potter and Wilkinson, unpublished work.
[14] Dave, Evans, and Wilkinson, *J.*, 1959, 3684.
[15] Fritz and Fischer, *J.*, 1961, 547.

evidence for or against an angular configuration. (A similar conclusion was reached [14] for the tin and lead compounds, even from solution spectra where the spectra were independent of the nature of the solvent.) It may be noted also that the reliability of intercomparisons of the spectra of the hydride species may be suspect because there are differences in the structure of the species—neutral compounds and salts, different numbers of hydrogen atoms, and valency of the metal atom—all of which could well complicate the interpretation of solid-state spectra.

Experimental

Microanalyses are by the Microanalytical Laboratory of this College. Preparations and operations were carried out under oxygen-free nitrogen or in a vacuum.

Di-π-cyclopentadienyltantalum Trihydride.—Anhydrous, freshly sublimed tantalum pentachloride (36 g., 0·1 mole) was slowly added to an ice-cooled solution of sodium cyclopentadienide (0·7—0·8 mole) in tetrahydrofuran (250 ml.) containing sodium borohydride (10 g.). The mixture was stirred for 4 hr. under reflux. After removal of the solvent in a vacuum the product was sublimed from the residue (*ca.* 120°/10^{-2} mm.) and purified by resublimation at 100° as white crystals, m. p. 187—189° (decomp.) (Found: C, 37·0; H, 4·0. $C_{10}H_{13}Ta$ requires C, 38·2; H, 4·2%). The preparation does not always succeed, but the reasons for failure are not clear; on occasion we have experienced yields of the order of 60% based on tantalum metal.

Di-π-cyclopentadienylmolybdenum Dihydride.—The reaction was carried out as above, but with molybdenum pentachloride (27 g.), sodium cyclopentadienide (0·5 mole), and sodium borohydride (10 g.). The product was sublimed from the residue and crystallised from diethyl ether–light petroleum (b. p. 40—60°) at −78°. An alternative method of isolation is that used for the rhenium hydride [1] where the dry residue is treated with 3N-hydrochloric acid. After filtering, the solution is neutralised with 2N-sodium hydroxide, and the liberated hydride extracted with ether. The product was purified by vacuum-sublimation at 50°, to give yellow crystals (*ca.* 50% based on molybdenum), m. p. 183—185° (Found: C, 51·0; H, 5·3. $C_{10}H_{12}Mo$ requires C, 52·7; H, 5·3%).

Di-π-cyclopentadienyltungsten Dihydride.—A similar procedure but with tungsten hexachloride (40 g.), sodium cyclopentadienide (0·6 mole), and sodium borohydride (10 g.) led to yellow crystals (*ca.* 65% based on tungsten), subliming in a vacuum at 80° and having m. p. 163—165° (Found: C, 38·2; H, 3·9. $C_{10}H_{12}W$ requires C, 38·0; H, 3·8%). The tungsten compound is moderately stable in air and after about 15 min. in air about half of the material can be recovered.

Di-π-cyclopentadienylmolybdenum and Tungsten Trihydride Salts.—The dihydrides were treated with gaseous hydrogen bromide at room temperature as for the rhenium compound.[1] The yellow crystals rapidly disintegrated, leaving white, very hygroscopic solids. In presence of excess of hydrogen bromide, the solids are pink [cf. $(\pi\text{-}C_5H_5)_2ReH_2Br$].

Aqueous solutions of the cations are obtained by dissolving the bromides in water or by dissolving the dihydrides in aqueous acid. The aqueous solutions are similar to those of $(\pi\text{-}C_5H_5)_2ReH_2^+$ [1] and give precipitates with large anions. On addition of base, the dihydrides are liberated quantitatively. The dihydrides readily dissolve in pure trifluoroacetic acid to solutions containing the trihydride ions; the molybdenum solution is green and the tungsten olive green.

The dideuterides and trideuteride ions can be obtained by the previous procedure,[1] by dissolution of the dihydrides in 2N-deuterium chloride, followed by neutralisation with sodium deuteroxide in deuterium oxide.

Infrared Spectra.—Measurements were made with a Perkin-Elmer model 21 spectrophotometer with sodium chloride optics and a Grubb-Parsons grating spectrophotometer in the region of the M–H stretching frequencies. The molybdenum and tungsten dihydrides were measured in CS_2 solutions and in Nujol mulls; mull spectra only were obtained for the tantalum trihydride.

$(\pi\text{-}C_5H_5)_2MoH_2$: 3060 (w), 1847 ± 2 (Mo–H str., ms), 1415m, 1369m, 1267m, 1121ms, 1064ms, 1055ms, 869w, 813m, 763s.

$(\pi\text{-}C_5H_5)_2WH_2$: 3050 (w), 1896 ± 2 (W–H str., ms), 1410m, 1257m, 1088m, 998m, 885w, 799m, 769m.

$(\pi\text{-}C_5H_5)_2TaH_3$: 3090 (w), 1735 ± 2 (Ta–H str., vs), 1425m, 1358w, 1265w, 1117w, 1072w, 1020s, 1005s, 905m, 870s, 858m, 848m, 825s, 795s, 720w.

High-resolution Nuclear Magnetic Resonance Spectra.—Measurements were made on a Varian Associates model 4300B spectrometer at 56·4 Mc./sec. and 22° ± 2°. The neutral hydrides were studied in strong solutions in benzene while the trihydride cationic species were measured in water and also in trifluoroacetic acid, tetramethylsilane then being added as an internal reference. Line positions were determined by conventional side-band techniques.

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956. *Nitration of the* N-*Acyl-nitronaphthylamines.*

By E. R. Ward and P. R. Wells.

The nitration of some *N*-acyl derivatives of all fourteen mononitronaphthylamines has been studied under a variety of conditions. Comparisons of their reactivity and mode of substitution with those of the parent naphthylamines have permitted the formulation of some general conclusions regarding substituent effects. Anomalous orientations observed for nitration of *N*-acetyl derivatives in strongly acidic media are rationalised in terms of protonation of the amide-oxygen atom of the acetyl group.

A study of the nitration of some of the *N*-acyl derivatives of all the nitronaphthylamines is here presented. From the position and extent of reaction and the distribution of isomers a clear picture emerges of the effect of the acylated amino-group and the influence of the nitro-group at various positions. The latter is particularly interesting and depends upon the fact that orientation in these compounds is controlled by the amido-substituent. The nitro-group alone, as in the nitronaphthalenes,[1] permits reaction to occur detectably only in the α-positions of the unsubstituted ring, thus somewhat limiting the information that can be derived.

The mildest nitrating condition employed in these studies has been nitric acid in acetic acid solution. This reagent is effective only for the more reactive substrates, the sulphonyl derivatives and the parent *N*-acetylnaphthylamines. On addition of boron trifluoride, however, *N*-acetyl-dinitro-compounds are obtained. In fuming nitric acid (which in favourable cases leads to the formation of trinitronaphthylamine derivatives), there are abnormal results ascribed to protonation.

The mononitration of the *N*-acetyl derivatives has proved the most informative of these investigations. The α-derivatives react in the 2- and the 4-position; the β-derivatives at positions 1, 6, and 8, the ratios in which the products are formed depending on the position of the nitro-group. The more reactive *N*-arylsulphonyl derivatives have proved extremely difficult to mononitrate: the significance of the composition of the resulting product is thus difficult to interpret; study of these derivatives has, however, been of value in the synthesis of otherwise inaccessible compounds. The *N*-phthaloyl derivatives have similarly provided new isomers, but they could not be studied quantitatively owing to the lack of a satisfactory method of hydrolysis.

In previous studies of these nitrations the usual procedure has been to permit the product to crystallise from the reaction medium, thus obtaining fairly pure material immediately. While this is useful in preparative work it was necessary for the present

[1] Ward, Johnson, and Day, *J.*, 1959, 487.

investigation to examine the whole reaction product. In order that the final isomer distribution shall be significant, yields at all stages should be high and the by-products that are carried through to the final stage efficiently separated from the nitro-amines.

TABLE 1.

Nitration of *N*-acetyl derivatives in acetic acid.

Expt. no.	Position of NHAc	Position of NO_2	Reagent & temp.	Yields (%) I	Yields (%) II	Yields (%) III	Posn. of substn., refs., notes
1	1	—	A, 0°	87	96	76	2; 4 *
2	1	—	B, 70	82	95	76	2; 4
3	1	3	B, 70	86	—	61 *	2; 4 (*a*)
4	1	5	B, 70	79	91	66	2; 4
5	1	8	B, 80	30		18	2; 4
6	2	—	A	81	—	—	1; 6; 8 (*b*)
7	2	—	B, 70	63	84	47	1; 6; 8
8	2	3	B, 70	83	100	75	1; 6; 8 (*c*)
9	2	4	B, 70	81	83	54	1; 6

Reagents: A, HNO_3 (*d* 1·5) in acetic acid. B, HNO_3 (*d* 1·5) and BF_3 in acetic acid. C, HNO_3 (*d* 1·5) alone.

Yields: I, Crude nitration product. II, Crude hydrolysis product. III, Purified and separated hydrolysis product. I and II are yields referring to the particular operation. III is a combined overall yield in relation to starting material. Separation and purification by chromatography of the hydrolysis product was generally the step of highest yield.

References: (*a*) Cf. Sihlbom, *Acta Chem. Scand.*, 1954, **8**, 1709. (*b*) Saunders and Hamilton, *J. Amer. Chem. Soc.*, 1932, **54**, 636; Hartman and Smith, *Org. Synth.*, Coll. Vol. II, p. 438. (*c*) Ward, Coulson, and Wells, *J.*, 1957, 4816.

* Similar yields reported by Hodgson and Walker (*J.*, 1933, 1205) using nitric acid (*d* 1·4) in acetic acid and in acetic anhydride.

TABLE 2.

Nitration of *N*-acetyl derivatives in nitric acid.

Expt. no.	Position of NHAc	Position of NO_2	Reagent & temp.	Yields (%) I	Yields (%) II	Yields (%) III	Posn. of substn., refs., notes
10	1	—	C, 0°	74	93	—	2,4; 4,5; & 4,8 *
11	1	2	C	—	—	—	4,8
12	1	3	C, 0	80	98	87	5; 8 [d]
13	1	4	C, 0	87	90	67	2; 5; 8 †
14	1	5	C, 0	97	93	74	2; 4 ‡
15	1	6	C, 0	88	99	80	2; 4
16	1	7	C, 0	97	90	62	2; 4 [e]
17	1	8	C, 0	92·5	—	—	2; 4 ¶
18	2	—	C	—	—	—	1,5; 1,8
19	2	1	C, 0	90	—	—	6,8
20	2	1	C	—	—	—	5; 8 [f]
21	2	3	C, 0	72	100	65	1,5; 1,8 [e]
22	2	4	C, 0	81	62	29	1,5; 1,8
23	2	5	C, 0	—	—	—	1 [f]
24	2	6	C, 0	—	—	—	1 [g]
25	2	7	C, 0	95	—	—	1 [h]
26	2	8	C, 0	—	—	—	1 [f]

References: (*c*) See Table 1. (*d*) Ward, Coulson, and Hawkins, *J.*, 1957, 4541. (*e*) Hardy and Ward, *J.*, 1957, 2634. (*f*) Vesely and Jakes, *Bull. Soc. chim. France*, 1923, **33**, 942. (*g*) Bell, *J.*, 1929, 2784. Hodgson and Ward, *J.*, 1947, 1060.

* Hodgson and Walker (*J.*, 1933, 1205) report 2- and 4-nitration at 10° by HNO_3 (*d* 1·4). † Lellman (*Ber.*, 1884, **17**, 114) reports 2-nitration only. ‡ By Mr. H. Pierce. ¶ Hodgson and Crook (*J.*, 1936, 1338) report 4-nitration only.

Discussion.—The principal results are summarised in Tables 1—6. In the nitration of acetanilide $p : \frac{1}{2}o$ ratios of great variety are observed depending on the nitration conditions.[2] Thus the ratio falls from 8 : 1 in mixed acid through various values of >1 : 1 for aqueous nitric acid to 0·9 : 1 for nitric acid in acetic anhydride. The ratio for positions 4 and 2 of *N*-acetyl-1-naphthylamine is, by comparison, remarkably constant. In addition

[2] Hodgson and Crook, *J.*, 1936, 1844.

TABLE 3.

Nitration of *N*-arylsulphonyl derivatives.

Expt. no.	Position of NHX	Position of NO_2	X *	Reagent & temp.†	Yields I (%)	Posn. of substn., refs., notes
27	1	—	T	A, 20°	100	4; 2,4
28	1	—	T	2A, 20	85	2,4
29	1	—	M	B, 0	—	2,4,5 [i]
30	1	3	T	A, 0	83	2; 4
31	1	3	T	2A, 0	—	2,4 [j]
32	1	5	T	A, 0	—	2; 2,4 ‡
33	1	5	T	2A, 0	65	2,4‡
34	1	6	T	A, 0	95	2; 4; 2,4
35	1	6	T	2A, 90	53	2,4 [k]
36	1	7	T	A, 0	92	2; 4 [e]
37	1	7	T	2A, 0	67	2; 2,4 [e]
38	1	8	T	2A, 80	58	2,4 [l]
39	2	—	T	A, 0	—	1 [m]
40	2	—	T	2A, 0	—	1,6 [g]
41	2	—	M	B, 0	—	1,6; 1,8; 1,6,8
42	2	1	T	A, 60	90	6
43	2	3	T, M	2A, 80	84	1 [e]
44	2	3	M	B, 0	90	1,6 [e]
45	2	4	T	A, 70	—	1 [n]
46	2	4	T	2A, 80	—	1,6 [n]
47	2	5	T	A, Warm	—	1 [g]
48	2	6	T	A	—	1 [g]
49	2	6	M	B	—	1,8 [g]
50	2	7	T	5A, 70	50	1 [h, o]
51	2	7	M	B, 35	—	1,5 [o]; 1,5(?)
52	2	8	T	A	—	1 [g]
53	2	8	M	B	—	1,6 [g]

References: (*c*) See Table 1. (*e*, *g*, *h*) See Table 2. (*i*) Consden and Kenyon, *J.*, 1935, 1591. (*j*) Hodgson and Hathaway, *J.*, 1945, 841. (*k*) Hodgson and Turner, *J.*, 1943, 391. (*l*) Ward and Day, *J.*, 1951, 782. (*m*) Morgan and Micklethwait, *J.*, 1912, **101**, 1438. (*n*) Hodgson and Hathaway, *J.*, 1945, 453. (*o*) Hodgson and Dean, *J.*, 1950, 818.

* T = Toluene-*p*-sulphonyl, M = *m*-nitrobenzenesulphonyl derivative. † 2A, 5A, etc., refer to the number of mol. of nitric acid employed. ‡ By Mr. H. Pierce.

TABLE 4.

Nitration of *N*-phthaloyl derivatives.

Expt. no.	Position of NPh	Position of NO_2	Yields (%) I	Yields (%) II	Yields (%) III	Posn. of substn., refs., notes
54	1	—	—	—	—	4; 5; 8 (1 : 6 : 12) [x]
55	1	—	86	62	35	4; 5; 4,8 (1 : 1) *
56	1	3	60	—	—	Dinitrated *
57	1	4	91	70	—	5; 8 *
58	1	7	90	—	—	2; 4; 4,5 (1 : 4 : 4) *
59	2	—	80—90	—	—	5; 8 [l]
60	2	1	90	77	57	6,8 *
61	2	3	100	—	—	5; 8 [c] (1 : 1)
62	2	4	100	90	59	5; 8 (1 : 1)
63	2	6	—	—	—	1; *x*; *y* (9 : 2 : 1) †

References: (*c*) See Table 1. (*l*) See Table 3. (*x*) Ref. 2.

* Nitration conducted for several hours. † By Mr. J. G. Hawkins.

to the values given in Table 5, Hodgson and Walker [3] report that nitration in acetic anhydride gives the ratio 2·5 : 1. This constancy is a strong argument that the same nitrating species (the nitronium ion) is concerned in all these reactions. Small variations, in so far as they are real, can be attributed to changes in solvent and temperature. The lower ratio for the reaction catalysed by boron trifluoride would then be due to the decreased selectivity of the reagent at the higher temperature. In support of this the ratio of the logarithm (1·28 : 1) of the isomer ratios is essentially equal to the inverse ratio of the absolute temperatures (1·26 : 1).

[3] Hodgson and Walker, *J.*, 1933, 1205.

TABLE 5.

4-Nitration/2-nitration of *N*-acetyl-1-naphthylamines.

Expt. no.	Position of NHAc	Position of NO_2	Conditions * A	Conditions * B	Conditions * C †
1, 2	1	—	2·9 ± 0·05	2·3 ± 0·05	2·7
3	1	3	—	*ca.* 4	—
4, 14	1	5	—	1·2 ± 0·02	2·6 ± 0·1
15	1	6	—	—	2·0 ± 0·15
16	1	7	—	—	1·7
5, 17	1	8	—	*ca.* 30	*ca.* 18·5

* See Experimental section for estimation of accuracy. † For HNO_3 (*d* 1·4) at 10° by thermal analysis (ref. 3).

TABLE 6.

Proportions of nitration at positions 1, 6, and 8 of *N*-acetyl-2-naphthylamines.

Expt. no.	Position of NHAc	Position of NO_2	Conditions	Proportions 1	Proportions 6	Proportions 8
6	2	—	A	51	4	5
7	2	—	B	*ca.* 9	1	—
8	2	3	B	15	2	3
9	2	4	B	*ca.* 17·5	1	—

The high p : $\frac{1}{2}o$ ratios for acetanilide have been variously explained in terms of specific *para*-activation [4,5] or of specific *ortho*-deactivation,[4,5] or as a direct consequence of the mode of operation of $+M$, $-I$ substituents.[6,*] These considerations should apply equally to *N*-acetyl-1-naphthylamine; in addition the greater reactivity of the α- than of the β-position should lead to an even higher proportion of 4- : 2-nitration. That these proportions are in fact smaller, except for nitration in acetic anhydride, indicates considerable steric effect due to the *peri*-hydrogen atom.

Table 5 indicates that, while 5, 6, and 7-nitro-groups have relatively little effect upon the 4- : 2-nitration ratio, an 8-nitro-group greatly reduces the amount of 2-nitration. This is an unusual steric effect. The nitro-group is not here affecting the reaction centre directly but by " buttressing " the effect of the acylated amino-group. This feature has been reported by Brown and McGary [7] for 2,3,5-tri- and 2,3,5,6-tetra-methylbenzene and will be more important for the naphthalenes owing to the close proximity of the *peri*-position. We have drawn attention above to the steric hindrance to nitration at the 4-position, so that the slightly increased ratio of 4- : 2-nitration of *N*-acetyl-5-nitro-1-naphthylamine is surprising when compared with the ratios for the 6- and the 7-nitro-isomer; an explanation of this has been presented [8] in terms of dipolar activation by the nitro-group.

The isomer ratios for the nitro-2-naphthylamines generally could not be determined with precision comparable to those mentioned above. It is of preparative interest that nitration of *N*-acetyl-2-naphthylamine in acetic acid is best carried out by the procedure of Hartman and Smith [9] but with only a 10% excess of nitric acid; [10] this affords a ~80%

* Unusually low p : $\frac{1}{2}o$-ratios for nitrations in acetyl nitrate have been explained by Norman and Radda (*Proc. Chem. Soc.*, 1960, 423) in terms of reaction of the nitrating agent with the substituent before substitution and by Bordwell and Garbisch (*J. Amer. Chem. Soc.*, 1960, **82**, 3588) in terms of some reagent other than the nitronium ion.

[4] Ingold, *Ann. Reports*, 1926, **23**, 140.
[5] Ingold, " Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N.Y., 1951, pp. 256—267.
[6] Dewar, *J.*, 1949, 463; Roberts and Streitweiser, *J. Amer. Chem. Soc.*, 1952, **74**, 4723; R. D. Brown, *J. Amer. Chem. Soc.*, 1953, **75**, 4077.
[7] H. C. Brown and McGary, *J. Amer. Chem. Soc.*, 1955, **77**, 2310.
[8] Wells and Ward, *Chem. and Ind.*, 1958, 1172.
[9] Hartman and Smith, *Org. Synth.*, Coll. Vol. II, p. 438.
[10] Ward and Hawkins, unpublished work.

yield of mixed *N*-acetyl-nitro-2-naphthylamines, which, on hydrolysis, yield 1-, 6-, and 8-nitro-2-naphthylamine in approximate ratios 9·8 : 1 : 1·25.[10] We have repeatedly obtained this result, in contrast to Saunders and Hamilton;[11] further, the material remaining in the nitration mixture after removal of the precipitated mixed products appears to be entirely *N*-acetyl-1-nitro-2-naphthylamine.

The results in Table 6 accord well with the predicted substituent effect of the 2-acetamido-group in that the 1-position is the most reactive although 6- and 8-activation is quite marked.

In nitric acid solution most of the homonuclear-substituted derivatives show a tendency to nitration at positions 5 and 8, *i.e.*, in the unsubstituted ring (sometimes accompanied by reaction in the substituted ring). This type of behaviour is well known for naphthalene compounds and is normally associated with the presence of a deactivating substituent. That it occurs only in strongly acidic conditions points to protonation as the cause.[12] The acetamido-group could take up a proton at either the nitrogen or the acetyl-oxygen atom. In the former case a substituent resembling the strongly deactivating NH_3^+ group would be produced. This seems unlikely because, first the *N*-protonated derivatives should be less reactive than the dinitronaphthalenes which cannot be nitrated under these conditions, and, secondly, both α- and β-naphthylammonium salts undergo more 5- than 8-nitration,[13] unlike the " abnormal " acetyl reactions where the reverse is often true. As will be seen for the *N*-phthaloyl derivatives and as is known[14] for the methylnaphthalenes, a deactivating substituent is not essential for reaction at position 5 or 8. A very weakly activating or deactivating substituent, such as would be produced by protonation of oxygen, will be able only to give direction to a choice among the available α-positions. Whether reaction occurs through the protonated amide or not will depend upon a number of factors. The unprotonated form being considerably more reactive must be in extremely low concentration, otherwise reaction would proceed almost entirely through this form. This is another argument against *N*-protonation, which would cause much more deactivation so that a trace of unprotonated derivative would provide for all the reaction. This condition being fulfilled, the protonated derivative must still be sufficiently reactive to be nitrated. It can be seen from Table 2 that a nitro-group in the second ring prevents the " abnormal " reaction by making the compound too unreactive. *N*-Acetyl-1-naphthylamine and its 4-nitro-derivative show behaviour consistent with the above analysis in that both normal and " abnormal " reactions are observed.

The 6,8-dinitration of *N*-acetyl-1-nitro-2-naphthylamine is unexpected. *N*-Acetyl-6- and -8-nitro-2-naphthylamine are only mononitrated under these conditions, yielding products at least one of which must be intermediate in the formation of the 1,6,8-trinitro-compound. In mixed acid the 1,5- and 1,8-dinitro-compounds are obtained, in conformity with the general behaviour of the other homonitro-isomers and *N*-acetyl-2-naphthylamine itself.

In contrast to the apparently stronger electron-withdrawing power of the arylsulphonyl group,[15] the *N*-toluene-*p*-sulphonyl derivatives are more easily nitrated than the *N*-acetyl derivatives. All the 1-naphthylamine derivatives having positions 2 and 4 vacant can be dinitrated in hot acetic acid. To avoid nitration of the arylsulphonyl group, *N*-*m*-nitrobenzenesulphonyl derivatives were nitrated in nitric acid. Under these more vigorous conditions the 2-naphthylamine derivatives are also dinitrated. The comparable reactivities of the 2- and the 4-position and of the mononitration products of the 1-naphthylamine derivatives lead in general to a mixed product. For the 2-naphthylamine derivatives, on the other hand, the differences are sufficient for mononitration to be confined to the 1-position. Contrasting with the *N*-acetyl derivatives, the sulphonyl derivatives

[11] Saunders and Hamilton, *J. Amer. Chem. Soc.*, 1932, **54**, 636.
[12] Ward and Coulson, *J.*, 1954, 4541; Ward, Coulson, and Wells, *J.*, 1957, 4816.
[13] Hodgson and Davey, *J.*, 1939, 348; Finelli, U.S.P., 2,790,831, *Chem. Abs.*, 1957, **51**, 14,815.
[14] Wells and Alcorn, unpublished work.
[15] Cf. Hammett's σ-values, Jaffé, *Chem. Rev.*, 1953, **53**, 191.

have further reactivities in the order 6 > 8. 1,8-Dinitration is observed for the 6-nitro-derivatives only. Steric hindrance presumably prevents reaction of the 5-nitro-derivative at the 6-position and would be expected to affect the 7-nitro-isomer similarly. It has been suggested therefore that the dinitration of this latter compound occurs in the 1,5-positions.

While the *N*-phthaloyl derivative of aniline undergoes nitration in the *ortho*- and *para*-positions, the corresponding derivative of *p*-toluidine reacts at the *ortho*-position to the methyl group.[16] The substituent is thus at best very weakly activating or, more probably, weakly deactivating, being *o*/*p*-directing by virtue of a $+M$-effect. The result of this appears in Table 4 where it can be seen that reaction in the 5- and the 8-position (unsubstituted ring) competes favourably with that at positions appearing from the studies of the other derivatives to be normally activated by the acylated amino-group. In view of the unsatisfactory nature of the hydrolysis and subsequent separation of the nitration products, the ratio of isomers given has little significance. Noteworthy, however, is that 8-substitution in not unfavourable despite the bulk of the acyl group. Reactions of the 7-nitro-derivative at positions 2 and 4, and of the 6-nitro-derivative at position 1 accord with the suggested $+M$-effect of the substituent, since in these cases a nitro-group in the second ring will deactivate positions 5 and 8.

Viewed overall, the nitrations of the various naphthylamine derivatives are in good agreement with the analysis of the effect of substituents on electrophilic substitution in naphthalene, as set out by Ward, Coulson, and Wells.[12] Only in the presence of a strongly activating *o*/*p*-directing group does reaction take place in the β-positions of the naphthalene system. In other cases the preference for α-reaction has control and the substituent affects only the choice between available α-positions. The nitro-group does not appear to exert a very specific effect, except on positions adjacent to it and remote from the activating group: in accordance with its predominant inductive effect [17] overall deactivation appears to be the best description of its influence. There is, in addition, however, evidence that the position *peri* to the nitro-group is not unfavourable, as observed in the nitronaphthalenes.

Experimental

The derivatives used in these studies were prepared by established procedures and purified by crystallisation. M. p.s are corrected.

New N-*phthaloyl derivatives* are tabulated ($C_{18}H_{10}O_4N_2$ requires C, 67·9; H, 3·2; N, 8·8%).

Nitro-*N*-phthaloylnaphthylamines.

Position of			Found (%)		
N	NO_2	M. p.	C	H	N
1	5	230°	67·4	3·0	8·9
2	4	263	68·2	3·6	—
2	6 *	305	65·8	3·4	8·0

* Prepared by Mr. J. G. Hawkins.

Nitration: General Procedures.—(A) The *N*-acetyl derivative (1·0 g.) in glacial acetic acid (20 c.c.) was treated with nitric acid (*d* 1·5; *ca.* 1 c.c. excess) and left at the reaction temperature for *ca.* 30 min. Addition of ice (*ca.* 200 g.) produced a fine precipitate which was collected, washed with water, and dried at *ca.* 50° *in vacuo*.

(B) The *N*-acetyl derivative (1·0 g.) in acetic acid (50 c.c.) was treated with a mixture of nitric acid (*d* 1·5; 0·24 g.) and a 40% solution (2 c.c.) of boron trifluoride–acetic acid complex in acetic acid (2·4 c.c.). After *ca.* 15 min. at the reaction temperature, ice (*ca.* 500 g.) was added, yielding the product as a precipitate that was worked up as in (A).

(C) The *N*-acetyl derivative (1·0 g.) was dissolved by small additions to ice-cold nitric acid (*d* 1·5; 10 c.c.). After *ca.* 30 min. the brown solution was poured on ice (*ca.* 200 g.), to yield the product as a precipitate. The arylsulphonyl and phthaloyl derivatives were nitrated analogously.

[16] Brady, Quick, and Welling, *J.*, 1925, **127**, 2264.
[17] Wepster, *Rev. Trav. chim.*, 1956, **75**, 1473.

Hydrolysis: General Procedures.—The nitrated *N*-acetyl derivatives (0·5 g.) were hydrolysed by 2 hours' refluxing in 10 c.c. each of 50% v/v aqueous sulphuric acid and ethanol; then an excess of cold dilute ammonia solution was added. The precipitated amines were collected, washed, and dried at *ca.* 50° *in vacuo*.

The nitrated arylsulphonyl derivatives (0·5 g.) were dissolved in sulphuric acid (*d* 1·84; 10 c.c.) and kept at *ca.* 40° for 4 hr., the solution was poured on ice (*ca.* 200 g.). The product was collected, washed, and dried at *ca.* 50° *in vacuo*.

Of the methods described for hydrolysis of the *N*-phthaloyl derivatives, *e.g.*, 2N-aqueous sodium hydroxide,[16] ammonia at 120—130°,[2] ethanolic mineral acid,[18] and ethanolic hydrazine,[19] only the last was generally successful and even then, in many cases, gave poor yields of impure product.

The crude hydrolysis product (0·5 g.) was chromatographed in benzene on alumina (a column of 2·6 × 30 cm.; 50 cm. for 2- and 4-nitro-1-naphthylamine, and for separation of 1- from 6- and 8-nitro-2-naphthylamine; the last pair and other pairs of mononitronaphthylamines were never completely separated). The various by-products that had been carried through to this final stage were adsorbed at the top of the column and did not interfere with recovery of purified nitro-amines.

Nitronaphthylamines and their acetyl derivatives.

		Amine				Acetyl derivative			
Position of			Found (%)				Found (%)		
NH_2	NO_2	M. p.	C	H	Notes	M. p.	C	H	Note
1	2,5	243°				242°			
1	2,6	318	51·5	3·0	*a*, *b*	270	52·5	3·85	*g*
1	2,8	166					—	—	—
1	4,6	250	51·5	2·9	*b*, *c*	256	50·4	4·4	*g*
2	1,4	161	51·0	3·0	*b*	—	—	—	
2	4,6	204	52·7	4·0	*b*	—	—	—	
2	4,8	268	52·2	3·4	*b*	—	—	—	
2	1,4,5	203	—	—	*d*, *e*	239	45·2	2·7	*h*
2	1,4,8	171	43·2	2·25	*e*, *f*	215	44·9	2·6	*i*

[a] Hodgson and Turner (*J.*, 1943, 391) give m. p. 228·5°. [b] $C_{10}H_7N_3O_4$ requires C, 51·5; H, 3·0%. [c] *Idem*, *loc. cit.*, give m. p. 178°. [d] Found: N, 20·0%. [e] $C_{10}H_8N_4O_6$ requires C, 43·2; H, 2·25; N, 20·2%. [f] Found: N, 19·8%. [g] $C_{12}H_9N_3O_3$ requires C, 52·4; H, 3·3%. [h] $C_{12}H_8N_4O_7$ requires C, 45·0; H, 2·5%; N, 17·5%. [i] Found: N, 17·5%.

To assess the accuracy of the separation 3 : 1 mixtures of any intermediate mixed fraction were added to the weights of pure isomer obtained. This gave two extreme values for the isomer ratio which were averaged and the extremes indicated in the form of a possible deviation. This procedure was only applied where nitration, hydrolysis, and separation yields were high.

Characteristics of New or Improved Compounds.—See annexed Tables.

Orientation of New Products.—On deamination by Hodgson and Turner's method,[20] 2,6-dinitro-1-, 4,6-dinitro-1-, 1,4-dinitro-2-, and 4,8-dinitro-2-naphthylamine gave, respectively, 2,6-, 1,7-, 1,4-, and 1,5-dinitronaphthalene, identified by mixed m. p. 1,4,5-Trinitro-2-naphthylamine was obtained from both 1,4- and 4,5-dinitro-2-naphthylamine, and the 1,4,8-isomer from the 1,4- and the 4,8-isomer. The structures of 2,8-dinitro-1- and 4,6-dinitro-2-naphthylamine, while not proved owing to an insufficiency of material, follow by analogy; the latter was shown by mixed m. p. determinations to differ from the 1,4-, 4,5-, and 4,8-isomer.

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[18] Hodgson and Dean, *J.*, 1950, 820.
[19] Hodgson and Ratcliffe, *J.*, 1949, 1314; Ward and Day, *J.*, 1951, 782.
[20] Hodgson and Turner, *J.*, 1942, 748; 1943, 68.

XUM

957. *The Bromination of the Nitronaphthylamines and their N-Acyl Derivatives.*

By E. R. Ward and P. R. Wells.

Molecular bromination of the nitronaphthylamines and of their *N*-acetyl and *N*-arylsulphonyl derivatives under a variety of conditions has been studied. The reactivity and mode of substitution of these compounds have been compared with those for the parent naphthylamines and with the results obtained in the corresponding nitration studies.[1] Mechanisms are suggested for results classified as abnormal.

The bromination of several of the nitronaphthylamines and their *N*-acyl derivatives has been reported previously, notably by Hodgson and his co-workers, but an overall picture of orientation and reactivity-determining factors could not previously be obtained. We now report results for all the nitronaphthylamines and their *N*-acetyl derivatives permitting a more detailed analysis.

Bromination of the *N*-acetyl derivatives is considered first since this may be compared with their nitration described earlier [1] and does not involve the abnormal reaction that apparently occurs in the bromination of the free amines in chloroform and other solvents. The solvent selected was 85% acetic acid since kinetic investigations [2] have been carried out in this medium, good yields of *N*-acetyl derivatives can be obtained by crystallisation from this solvent, and considerable amounts of sodium acetate can be introduced (to reduce developed acidity) without the reaction's becoming heterogeneous, and reactions can be carried out at *ca.* 100° without much loss of solvent. " Cold " conditions were used wherever possible, " hot " ones only for unreactive substrates.

Bromination of amines or substituted amines in chloroform solution has proved an excellent preparative method. The amines are readily soluble in the cold solvent; the hydrobromic acid liberated forms the insoluble hydrobromide of most of the product. This can be removed by filtration, usually in high yield, and invariably in a high state of purity since non-basic side-products remain in solution. For the present investigations it was essential that the whole product be examined; even so the amounts of by-products separated by chromatography were small. A few results for other solvents are available for comparison, as are others for temperatures above 20°; in no case was there any improvement; often yields were reduced.

Thirteen nitronaphthylamines and their *N*-acetyl derivatives have been studied. 1-Nitro-2-naphthylamine has been omitted since preliminary experiments indicated that its behaviour is unique and requires a separate study.

Only a few isomers among the *N*-arylsulphonamides were examined, in order to specify " normal " and " abnormal " brominations of these derivatives. Previous reports of bromination in pyridine have been confirmed, extended, and compared with the " normal " reaction observed in acetic acid. Yields of product from these derivatives were variable and rarely quantitative.

The following Tables list the results of the present and some previous investigations. A single entry under " yield " is that for purified reaction product, usually after chromatography in the case of the amine studies, but for unpurified product in the case of the derivatives. In all cases the yields were calculated on the basis of the composition determined subsequently.

Discussion.—Monobromination of the *N*-acetyl derivatives is readily brought about in the cold for those isomers not suffering strong deactivation by the nitro-group. In accordance with the greater selectivity of molecular bromine than of the nitronium ion,

[1] Ward and Wells, preceding paper.
[2] Brown and Stock, *J. Amer. Chem. Soc.*, 1957, **79**, 1421.

substitution in only one nuclear position is observed whereas nitration generally produces a mixture of isomers.[1] As our chromatographic method reveals the presence of >1% of a second isomer,[3] it can be estimated that the 4-position of the α-naphthylamine series and the 1-position in the β-series are the most reactive by a factor of at least 100. *N*-Acetyl-4-nitro-1-naphthylamine is, of course, an exception: it reacts in the only unoccupied reactive position, with difficulty. The 5-nitro-isomer is also unreactive, substitution occurring with difficulty in the 2-position, owing to a steric effect of the *peri*-nitro-group on the 4-position; it is pertinent that this substance gives an exceptionally high ratio of 4- : 2-nitration,[1] which was interpreted in terms of a dipolar activating effect that would not operate for the neutral reagent of bromination.[4] As would be expected from the deactivating effect of the nitro-group on the ring to which it is attached, the 2- and the 3-nitro-isomer are also unreactive, especially the latter where there are also serious steric restrictions. Vigorous conditions are required for the latter bromination. In the

TABLE 1.

Bromination of *N*-acetyl derivatives in aqueous acetic acid.

Position of NHAc	Position of NO_2	Br_2 (mol.)	Temp.*	Posn. of substitn.	Yield (%)	Notes & refs.
1	—	1	C	4	97	*a*
1	—	2	C	4	(107)	i
1	—	2	H	2,4	77	
1	2	1	C	4 †	80	ii
1	3	5	H	2; 2,4	46	iii
1	4	1	C	2 †	95	iv
1	5	1	H	2 †	85	iii
1	5	2	H	2,4 ‡	51	
1	6	1	C	4	93	
1	6	2	H	2,4	80	
1	7	1	C	4	84	v, *b*
1	7	2	H	2,4	76	v, *b*
1	8	1	H	4	80	vi, *c*
1	8	2	H	2,4	—	*c*
2	—	2	H	1	99	vii, *d*
2	3	1	C	1	96	*e*
2	4	1	H	1 †	87	viii
2	5	1	—	1	—	v, *f*
2	6	1	C	1	91	
2	7	1	C	1	77	

* C = At 20° or 0°; H = at 100°. † Also unchanged material. ‡ Also a trace of 2-bromo-derivative.

Notes: (i) High apparent yield may indicate some 5% of dibromination. (ii) 4-Substitution in glacial acetic acid reported by Hodgson and Elliott (*J.*, 1935, 1850). (iii) No reaction at 20°. (iv) 85% Yield of monobromo-compound at 100°. (v) In glacial acetic acid. (vi) Lower yield in aqueous acetic acid. (vii) The reported formation of the 1,6-dibromo-compound could not be repeated. (viii) Complete bromination was only achieved with an excess of reagent.

References: (*a*) Cf. Perconito, *Gazzetta*, 1935, **65**, 689. (*b*) Hardy, Ward, and Day, *J.*, 1956, 1979. (*c*) Hodgson and Crook, *J.*, 1936, 1338. (*d*) Cf. Consiner, *Ber.*, 1881, **14**, 58; Claus and Philipson, *J. prakt. Chem.*, 1891, **43**, 47. (*e*) Ward, Coulson, and Wells, *J.*, 1957, 4816. (*f*) Veselý and Dvorak, *Chem. Listy*, 1923, **17**, 163.

β-series reactivity differences can be distinguished only between *N*-acetyl-4-nitro-2-naphthylamine (which is unreactive) and the other isomers. In this compound the nitro-group is placed so that its greatest influence is felt at the reaction site, *i.e.*, the *para*-position. Even under the " hot " conditions the β-derivatives were not dibrominated. On the other hand, all the α-derivatives are sufficiently reactive for bromination at positions 2 and 4 (if free). " Cold " conditions do not, however, seem sufficient for this further reaction except perhaps in the case of *N*-acetyl-1-naphthylamine itself.

The outstanding feature of the bromination of the amines in chloroform is that although monobromination and, for some isomers, dibromination can be cleanly effected in the

[3] Cf. Ward, Johnson, and Day, *J.*, 1959, 487.
[4] Wells and Ward, *Chem. and Ind.*, 1958, 1172.

TABLE 2.

Bromination of nitronaphthylamines in chloroform solution.

Position of NH_2	Position of NO_2	Br_2 (mol.)	Temp.	Posn. of substitn.	Yield (%)	Notes & refs.
			(A) *Nitro-1-naphthylamines*			
1	—	1	20°	2,4 *	99	
1	—	2	20	2,4	88	i
1	2	1	20	4	—	ii, iii
1	3	1	20	2,4 *	98	
1	3	2	50	2,4	100	*g*
1	4	1	20	2	92·5	ii, iv
1	5	1	20	2; 2,4	92	v
1	5	2	20	2,4	100	vi
1	6	1	−5	2,4 *	58	*h*
1	6	2	−5	2,4	100	*h*
1	7	1	20	2,4 *	—	*b*
1	7	2	20	2,4	90	*b*
1	8	1	0	2,4 *	—	vii, *c*
1	8	2	0	2,4	100	vii, *c*
			(B) *Nitro-2-naphthylamines*			
					Yield (%) crude	pure
2	—	1	20	1	99	96
2	—	2	20	1,6	92	—
2	3	1	20	1	100	95	*e*
2	3	2	20	1,6	88	—	*e*
2	4	1	50	1	100	—	*i*
2	4	2	20	1,6	93	—	
2	5	1	20	1	92	89	viii
2	6	1	20	1	95	85	viii
2	7	1	50	1	90	—	viii, *j*
2	8	1	20	1	98	96	
2	8	2	20	1,6	80	—	

* Also unchanged material.

Notes: (i) Consden and Kenyon [k] report a quantitative yield in acetic acid at 100°. (ii) With an excess of bromine 2,4-dibromonaphthalene-1-diazonium perbromide is formed.[k] (iii) Similar results are reported for acetic acid or nitrobenzene solution.[l] (iv) 50% Yield in acetic acid at 100°; [k] 35% Yield in nitrobenzene at 20°.[m] (v) Hodgson and Turner [n] found only the 2-bromo-compound. (vi) Hodgson and Turner [n] report 58% yield at 50°. (vii) Similar results reported for carbon tetrachloride and nitrobenzene solutions. (viii) No dibromination even at 50°.

References: (*b*, *c*, *e*) See Table 1. (*g*) Hodgson and Hathaway, *J.*, 1944, 21. (*h*) Hodgson and Dean, *J.*, 1950, 822. (*i*) Hodgson and Hathaway, *J.*, 1944, 385. (*j*) Hodgson and Ward, *J.*, 1947, 327. (*k*) Consden and Kenyon, *J.*, 1935, 1591. (*l*) Hodgson and Elliott, *J.*, 1935, 1850. (*m*) Veselý and Chudozilov, *Chem. Listy*, 1925, **19**, 260; Hodgson and Elliott, *J.*, 1934, 1705. (*n*) Hodgson and Turner, *J.*, 1942, 723.

TABLE 3.

Bromination of *N*-*p*-toluenesulphonyl derivatives.

Position of NHTos	Position of NO_2	Solvent	Temp.	Posn. of substitn.	Yield (%)	Notes & refs.
1	—	Chloroform	" Cold "	4	" Good "	i, *k*
1	—	Pyridine	" Cold "	2,4	" Good "	*k*
1	3	Acetic acid	20°	4 *	84	
1	3	Pyridine	20	4; 2,4	80	
1	4	Chloroform	" Cold "	N.R.†		*k*
1	4	Pyridine	—	2	—	*k*
1	5	Acetic acid	20°	4; 2,4	90	ii
1	5	Pyridine	20	N.R.†	—	
1	8	Acetic acid	20	4	94	iii
1	8	Pyridine	20	N.R.†		
2	—	Chloroform	" Hot "	1,6	" Poor "	*o*
2	—	Pyridine	" Cold "	1,3	—	*o*
2	1	Pyridine	" Cold "	3	—	
2	6	Pyridine	" Cold "	1	" Good "	*j*
2	7	Pyridine	" Cold "	1	" Good "	*j*

* Also unchanged material. † No reaction.

Notes: (i) *N*-*m*-Nitrobenzenesulphonyl derivative. (ii) Whitehurst (*J.*, 1951, 222) reports a 10% yield of the 4-bromo-compound in acetic acid at 95°. (iii) *Idem* (*ibid.*) reports a 56% yield in acetic acid at 50°.

References: (*k*, *j*) See Table 2. (*o*) Belt, *J.*, 1932, 2732.

β-series, yet in the α-series, despite the use of a deficiency of reagent, the dibromo-compound is generally the only product obtained. This type of behaviour, classified as " abnormal," has been noted before, not only in bromination but also in other reactions.[5] One explanation,[5] which seems to be generally favoured, requires that the unsubstituted compound, being the stronger base, becomes protonated, and hence removed from reaction so much more completely than the monobromo-compound that reaction takes place preferentially through the latter. However, it has been shown [6] that even when the two brominations compete with equal rate constants the final reaction mixture contains comparable quantities of monobromo- and dibromo-compound and unchanged material. Hence to account for the experimental result of no detectable monosubstitution this type of explanation requires that decreased basicity must more than compensate for decreased reactivity. This seems most unlikely since the 2-position of these substrates must be less reactive than the 4-position (the *N*-acetyl results suggest a factor of at least 1/100), without account being taken of the deactivating effect of the bromine. The latter factor alone appears to make the explanation untenable since Hammett's ρ values indicate that reactivity towards bromination would be reduced more by a *m*-bromo-atom than basicity would be reduced by a *p*-bromo-atom ($\sigma_{p\text{-Br}} = 0{\cdot}23$; [7] $\sigma^*_{m\text{-Br}} = 0{\cdot}40$; [8] $\rho = 2{\cdot}77$ for the acid dissociation of the anilinium ions; [9] $\rho = -11{\cdot}35$ for halogenation in acetic acid [8]).

TABLE 4.

Bromination of other *N*-toluene-*p*-sulphonyl derivatives in pyridine.

NHTos	Position of X	Posn. of substitn.	Yield (%)	Refs.
1 *	4-Br	2	—	*k*
2 *	1,5-$(NO_2)_2$	3	83	*p*
2	1,6-$(NO_2)_2$	3	—	*k*
2	1-Cl	3	—	*q*
2	1-Br	3	—	*o*
2	1,6-Br_2	3	—	*o*

* *N*-*m*-Nitrobenzenesulphonyl derivative.

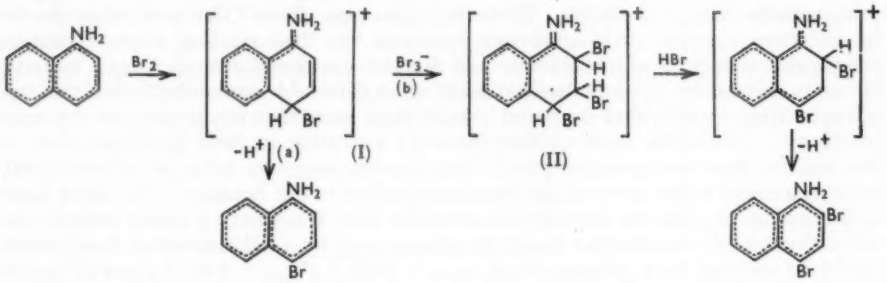
References: (*k*) See Table 2. (*o*) See Table 3. (*p*) Hodgson and Dean, *J.*, 1950, 820. (*q*) Bell, *J.*, 1950, 3035.

The results require that the formation of the 2,4-dibromo-compound shall be considerably faster than monobromination. Clearly this cannot be electrophilic substitution.

Clues to the nature of this reaction are provided by the bromination of the 3- and 5-nitro-amine and by the further reactions of the bromination products of the 2- and the 4-isomer. " Abnormal " behaviour is observed for 3-nitro-1-naphthylamine with no apparent reduction in reactivity despite the deactivating nitro-group (cf. the bromination of the *N*-acetyl derivative). 5-Nitro-1-naphthylamine, on the other hand, is the only member of the α-series that can be monobrominated, and here reaction occurs in the 2- instead of the usually more reactive 4-position. With an excess of bromine in chloroform, 4-bromo-2- and 2-bromo-4-nitro-1-naphthylamine are both converted into 2,4-dibromonaphthalene 1-diazoperbromide.[10] This product arises by nucleophilic displacement of the nitro-group as nitrite which subsequently, under the acid conditions, diazotises the amino-group. Such a displacement is not a usual reaction and requires the presence of some powerful nucleophilic bromide-ion equivalent, such as Br_3^-. These facts suggest a mechanism similar to that proposed by Robertson [11] for chlorination of 2-naphthol. It it is supposed that the first step is electrophilic bromination in the 4-position, to yield the intermediate (I), then nucleophilic addition (path b), the reagent being Br_3^-, could

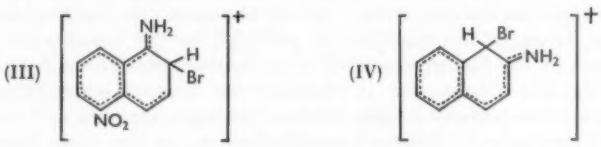
[5] de le Mare and Ridd, " Aromatic Substitution," Butterworths, London, 1959, pp. 48, 106.
[6] Wells, *J. Phys. Chem.*, 1959, **63**, 1978.
[7] McDaniel and Brown, *J. Org. Chem.*, 1958, **23**, 420.
[8] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1957, **79**, 1913.
[9] Jaffé, *Chem. Rev.*, 1953, **53**, 191.
[10] Consden and Kenyon, *J.*, 1935, 1591.
[11] Robertson, *J.*, 1956, 1883.

compete very favourably with the usual second step of proton loss (path a) and give the addition compound (II). Loss of hydrogen bromide and then a proton from the intermediate (II) would yield the 2,4-dibromo-compound. A highly nucleophilic bromide-containing species is present in the reaction mixture and a nitro-group would assist, instead of retarding, the key step in this mechanism. The intermediate (III) that will be



formed from 5-nitro-1-naphthylamine, which reacts first in the 2-position, would have a styrene-like structure instead of one having an activated 2,3-double bond as (I). It, and for the same reason the nitro-amines (IV) of the β-series, will tend to follow path a and yield monobromination products.

If the above considerations are correct, then the results for the β-series are for true electrophilic substitutions uncomplicated by addition–elimination. The 1-position, as indicated by the *N*-acetyl results, is so much the most reactive that only one monobromination product is detected. The next most reactive position is 6, and in dibromination this position (when unoccupied) will be the site of further substitution provided there is no "*ortho*"-nitro-group, as in the 5- and the 7-isomer. For bromination, unlike nitration, there is no indication of activation of the 8-position. Polar activation of positions 6 and 8 may be comparable but the *peri*-bromo-group would be expected effectively to block approach of the large bromine molecule to the latter reaction site.



Only a few selected *N*-arylsulphonamides were examined in these studies, principally to throw light on the effect of pyridine. Unusual orientation, specifically reaction in the 3-position of some β-derivatives, has been known for some time. Bell [12] suggested that pyridine abstracts a proton from the weakly acidic derivative, to yield a negatively charged nitrogen species that reacts readily with the polarized bromine in the presumably inductively activated 3-position. It would be expected, however, that such a substituent would activate the 6-position (where reaction normally occurs in other solvents) as strongly as, if not more strongly than, the 3-position, and thus lead to the usual product at a faster rate. Furthermore, reaction in the 3-position has not been observed for β-naphthyl oxides with, for example, diazotized amines. This almost unique orientation has been attributed [13] to a mechanism very similar to that suggested above for "abnormal" bromination of amines. The base, pyridine, facilitating the removal of hydrogen bromide from the addition product, will favour the addition–elimination mode of introduction of

[12] Bell, *J.*, 1950, 3035.
[13] Panizzon-Favre, *Gazzetta*, 1924, **54**, 838.

bromine. In support of this we have found that, while the *N*-toluene-*p*-sulphonyl derivatives of 3-, 5-, and 8-nitro-1-naphthylamine behave as do their *N*-acetyl derivatives in acetic acid, the 3-isomer is more reactive in pyridine than in acetic acid, while the 5- and the 8-isomer are more reactive in acetic acid. Presumably the addition–elimination mechanism is not operative for these two substances but can be utilised for readier reaction by the 3-isomer (and also the 4-isomer).

Experimental

M. p.s are corrected.

Bromination: General Procedures.—In chloroform. The nitronaphthylamine in cold chloroform (30 c.c./g.) was treated at room temperature (*ca.* 20°), with a 10% w/v solution of bromine in chloroform (8·6 c.c./g. for monobromination, or 17·1 c.c./g. for dibromination). The hydrobromide, which immediately began to separate, was collected after 24 hr. and washed with chloroform (5 c.c.). After removal of the chloroform *in vacuo*, this product was suspended in ice-water and treated with ammonia (*d* 0·88), to liberate the free amine. This material usually constituted 50—80% of the total product and was invariably of extremely high purity. The residual chloroform solution and washings yielded, on evaporation, the remaining bromoamine. In all experiments the two fractions were combined and chromatographed on alumina with benzene–ethyl acetate. All mixtures were readily separated; the minor amounts of by-products remained at the top of the columns.

In "cold" aqueous acetic acid. The *N*-acetyl or *N*-toluene-*p*-sulphonyl derivative (0·5 g.) was dissolved in the minimum of cold 85% v/v aqueous acetic acid (0·15M in sodium acetate) and treated at room temperature with the equivalent quantity of bromine (0·05M in the above solvent). The mixture was set aside for 24 hr. in a stoppered dark bottle, then the product was precipitated by addition of ice (in many cases considerable quantities of the product crystallised during the reaction). After being washed with water and dried at *ca.* 50° *in vacuo*, the products were hydrolysed as previously described [1] and chromatographed on alumina. The strongly adsorbed by-products were generally in greater, though still small, amounts than in bromination of amines in chloroform; products crystallising from the reaction solution were, however, always of high purity.

In "hot" aqueous acetic acid. The *N*-acetyl derivative (0·5 g.) was dissolved in the minimum of the warm solvent, heated on a boiling-water bath and treated dropwise with the reagent during 60—90 min. After a further 1—3 hr. at this temperature and ~12 hr. at room temperature, the mixture was worked up as described for the "cold" reaction. The crystalline material obtained on cooling was generally very pure, but chromatography of the hydrolysed material revealed appreciable quantities of by-products.

In pyridine. The *N*-toluene-*p*-sulphonyl derivative (1·0 g.) was set aside for 24 hr. with bromine (1·0 g., 2·1 equiv.) in pyridine, (25 c.c.). Addition to ice precipitated the product

Table 5.

Position of NH_2	Position of NO_2	Br	M. p.	Found (%) C	Found (%) H	Found (%) Br	Formula	Required (%) C	Required (%) H	Required (%) Br
Bromo-nitronaphthylamines										
1	3	2	113°	45·1	3·0	29·7	$C_{10}H_7BrN_2O_2$	45·0	2·3	29·9
1	6	4	214	45·1	3·0	—	,,	,,	,,	,,
2	4	1,6	177	—	—	46·3	$C_{10}H_6Br_2N_2O_2$	34·7	1·75	46·2
2	8	1,6	139	34·4	1·6	46·6	,,	,,	,,	,,
N-Acetyl-bromo-nitronaphthylamines										
1	3	2	246	—	—	26·0	$C_{12}H_9BrN_2O_3$	46·6	2·9	25·85
1	6	4	269	46·4	2·8	—	,,	,,	,,	,,

which was washed with dilute hydrochloric acid, followed by water, and dried at *ca.* 50° *in vacuo*. The sulphonamide was hydrolysed as previously described [1] and the resulting amine chromatographed on alumina.

New Compounds.—See Table 5. 4-Bromo-3-nitro-1-naphthylamine has m. p. 143°, and its *N*-toluene-*p*-sulphonyl derivative, m. p. 230°.

Orientations.—2-Bromo- was different (mixed m. p.) from 4-bromo-3-nitro-1-naphthylamine

obtained from N^1-acetyl-3-nitro-1,4-naphthylenediamine by Sandmeyer reaction as reported by Panizzon-Favre.[13] Both bromo-amines gave the 2,4-dibromo-compound on further bromination in chloroform. 4-Bromo-6-nitro-1-naphthylamine was diazotised by the method of Hodgson and Turner,[14] and the resulting diazonium solution added to a suspension of cuprous oxide in ethanol. After initial reaction had subsided, further cuprous oxide was added and the mixture left for 10 min. before addition to ice. The red-brown solids were dried and extracted with boiling benzene, to yield, by concentration and two recrystallisations, pale yellow needles, m. p. 132°, of 1-bromo-7-nitronaphthalene, undepressed on admixture with an authentic specimen. 1,6-Dibromo-8-nitro-2-naphthylamine was deaminated as above, to give *1,6-dibromo-8-nitronaphthalene* as buff needles, m. p. 97° (from benzene) (Found: C, 36·6; H, 1·7. $C_{10}H_5Br_2NO_2$ requires C, 36·3; H, 1·5%). This (0·1 g.) was ground with hydrated stannous chloride (1 g.) and cautiously warmed for 1 hr. with concentrated hydrochloric acid (2 c.c.). After dilution with cold water (50 c.c.), the solids were collected and air-dried for 2 days. Extraction with hot ethanol and evaporation gave 3,8-dibromo-1-naphthylamine as a brown semi-solid material that did not crystallise from the usual organic solvents. The crude bromoamine was dissolved in sulphuric acid (5 c.c.; *d* 1·84), diazotised, and deaminated as described above, to yield white crystals, m. p. and mixed m. p. 61°, of 1,6-dibromonaphthalene. Insufficient 1,6-dibromo-4-nitro-2-naphthylamine was available for similar reactions.

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[14] Hodgson and Turner, *J.*, 1943, 86.

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958. *Synthetic Studies relating to the Carbohydrate–Protein Linkage in Egg Albumin.*

By G. S. MARKS and A. NEUBERGER.

N-(L-β-Aspartyl)-β-D-glucopyranosylamine (Ia) and -D-glucosamine (IIa) have been prepared as models of corresponding derivatives possibly present in egg albumin. α-Benzyl benzyloxycarbonyl-L-aspartate (V) was made to react with tetra-*O*-acetyl-β-D-glucopyranosylamine (III) and -β-D-glucosamine (IV) in the presence of dicyclohexylcarbodi-imide, yielding 2,3,4,6-tetra-*O*-acetyl-*N*-(α-benzyl benzyloxycarbonyl-L-β-aspartyl)-β-D-glucopyranosylamine (Ib) and 1,3,4,6-tetra-*O*-acetyl-*N*-(α-benzyl benzyloxycarbonyl-L-β-aspartyl)-β-D-glucosamine (IIb), respectively. Removal of protecting groups afforded the glucopeptides (Ia) and (IIa). The stability of the *N*-acyl–glucosylamine linkage in (Ia) and of the amide linkage in (IIa) was studied.

THE preparation of a glycopeptide, containing all the sugar residues in crystalline egg albumin has recently been described.[1-3] The nature of the chemical bond linking the carbohydrate to the peptide is of particular interest, and likely structures for this bond were considered. On the basis of the available evidence it was suggested [1] that the most likely structure is that of a β-aspartyl-glycosylamine, although in the absence of direct proof other linkages such as that between an aspartic acid carboxyl group and an amino-group of glucosamine cannot be excluded. It is of interest that aspartic acid is the amino-acid implicated in the linkage of protein to carbohydrate in two other glycoproteins. Gottschalk [4] has obtained suggestive evidence that in ovine submaxillary gland mucoprotein the carbohydrate is joined through the reducing end of *N*-acetylglucosamine to the

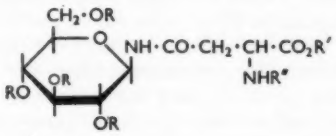
[1] Johansen, Marshall, and Neuberger, *Biochem. J.*, 1960, **77**, 239; 1961, **78**, 518.
[2] Cunningham, Nuenke, and Nuenke, *Biochim. Biophys. Acta*, 1957, **26**, 660.
[3] Jevons, *Nature*, 1958, **181**, 1346.
[4] Gottschalk, *Nature*, 1960, **186**, 949.

β-carboxyl group of aspartic acid by an ester linkage, and Rothfus [5] has evidence that in human serum γ-globulin there is a linkage between aspartic acid and glucosamine. The strength of the bond in the latter protein is indicative of an amide type of linkage which this author suggests might be between the amino-group of glucosamine and the β-carboxyl group of aspartic acid.

The aim of the present work was to synthesize *N*-(L-β-aspartyl)-β-D-glucopyranosylamine (Ia) and *N*-(L-β-aspartyl)-D-glucosamine (IIa) as models of corresponding derivatives possibly present in egg albumin, and to study their properties.

The *N*-acylglycosylamine structure is not novel amongst natural products as it is present in an intermediate in purine biosynthesis, *viz.*, glycine amide ribotide [*N*-glycyl-5′-phosphoribofuranosylamine (VI)].[6,7] Baddiley *et al.*,[8,9] in experiments directed towards the synthesis of this compound, have developed a general method for the synthesis of *N*-glycylglycosylamines. This consists of reaction between an *O*-acylated glycosylamine and benzyloxycarbonylglycyl chloride or benzyloxycarbonylglycyl ethyl carbonate, followed by removal of protecting groups. Thus the benzyloxycarbonyl compound (VII) was obtained by both the acid chloride and the carbonic anhydride route from tetra-*O*-acetyl-β-D-glucopyranosylamine (III) and benzyloxycarbonylglycine.

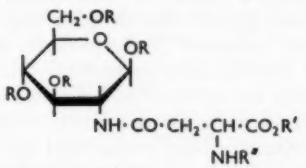
We have synthesized *N*-(L-β-aspartyl)-β-D-glucopyranosylamine (Ia) by a similar method *via* tetra-*O*-acetyl-*N*-(α-benzyl benzyloxycarbonyl-L-β-aspartyl)-β-D-glucopyranosylamine (Ib). The starting point was α-benzyl benzyloxycarbonyl-L-aspartate [10] (V). The preparation of this compound from benzyloxycarbonyl-L-aspartic anhydride calls for some comment since difficulty was experienced in obtaining a pure product by crystallization of the crude material. Le Quesne and Young [11] in a re-investigation of the reaction of benzyloxycarbonyl-L-aspartic anhydride with amino-esters and alcohols demonstrated



(Ia: R = R′ = R″ = H)

(Ib: R = Ac; R′ = CH_2Ph; R″ = O·CO·CH_2Ph)

(Ic: R = R′ = H; R″ = O·CO·CH_2Ph)

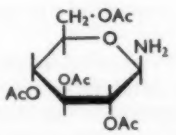


(IIa: R = R′ = R″ = H)

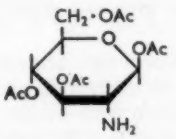
(IIb: R = Ac; R′ = CH_2Ph; R″ = O·CO·CH_2Ph)

(IIc: R = H; R′ = Me; R″ = O·CO·CH_2Ph)

(IId: R = Ac; R′ = R″ = H)



(III)



(IV)

that both α- and β-aspartyl derivatives can be formed. Owing to the closer proximity of the α-carboxyl group than of the β-carboxyl group to the benzyloxycarbonylamino-group, the β-isomer is the stronger acid and Le Quesne and Young were able to utilize this property

[5] Rothfus, *Fed. Proc.*, 1961, **20**, 383.
[6] Peabody, Goldthwait, and Greenberg, *J. Biol. Chem.*, 1956, **221**, 1071.
[7] Hartman, Levenberg, and Buchanan, *J. Biol. Chem.*, 1956, **221**, 1057.
[8] Baddiley, Buchanan, Handschumacher, and Prescott, *J.*, 1956, 2818.
[9] Baddiley, Buchanan, Hodges, and Prescott, *J.*, 1957, 4769.
[10] Bergmann, Zervas, and Salzmann, *Ber.*, 1933, **66**, 1288.
[11] Le Quesne and Young, *J.*, 1952, 24.

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to separate some of the isomers by fractional extraction of the mixture from an organic solvent with aqueous sodium carbonate. By utilizing this method of fractionation we were able to obtain pure α-benzyl benzyloxycarbonyl-L-asparate from the mixture of isomers. The rotation of this half-ester was in agreement with that reported by Bryant *et al.*[12] for this compound prepared by an alternative route. Recently, Dr. D. A. Lowther, working in our laboratory, has found a more convenient method of separation by utilizing an ion-exchange chromatographic procedure based on that of Busch, Hurlbert, and Potter [13] for the separation of organic acids. When the mixture of isomers was adsorbed on a strong-base resin in the acetate form, and the isomers were eluted with acetic acid of progressively increasing concentration, the two components were separated and both were recovered crystalline and in good yield.

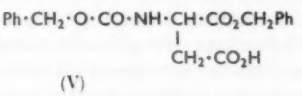
The next step involved the condensation of α-benzyl benzyloxycarbonyl-L-aspartate (V) with tetra-*O*-acetyl-β-D-glucopyranosylamine (III) to give the glucopeptide acetate (Ib). We obtained a good yield by using the carbodi-imide method of Sheehan and Hess [14] for this condensation. Treatment of the product (Ib) with lithium hydroxide in aqueous acetone caused simultaneous hydrolysis of the benzyl ester group and de-*O*-acetylation to the free acid (Ic). Removal of the benzyloxycarbonyl group by catalytic hydrogenation afforded the required *N*-(L-β-aspartyl)-β-D-glucopyranosylamine (Ia). It was of interest that this compound had a pK_2 value of 8·82 which is in close agreement with the pK_2 value of 8·80 reported for the α-amino-group of asparagine.[15] When the glucopeptide (Ia) was heated with the ninhydrin reagent of Moore and Stein [16] a brown colour was obtained identical with that obtained with asparagine.

The first synthesis of derivatives of D-glucosamine substituted on the nitrogen atom by acylamino-acid residues was carried out by Bergmann and Zervas.[17] They prepared tetra-*O*-acetyl-*N*-(benzyloxycarbonylglycyl)-β-D-glucosamine (VIIIa) by condensing benzyloxycarbonylglycyl chloride with tetra-*O*-acetyl-β-D-glucosamine (IV); removal of protecting groups afforded *N*-glycyl-D-glucosamine (VIIIb). Link and his co-workers,[18] utilizing this method, have prepared a series of *N*-acyl derivatives of D-glucosamine where the acyl groups are represented by amino-acid residues. They point out that the use of the acid chloride route for the synthesis of these derivatives suffers from the disadvantage that benzyloxycarbonylamino-acid chlorides are notably unstable, decomposing even below room temperature to benzyl chloride and an *N*-carboxy-amino-acid anhydride.[19] To overcome this disadvantage they attempted to acylate tetra-*O*-acetyl-β-D-glucosamine (IV) with acylamino-acylazides. However, the Curtius rearrangement occurred in every case investigated and this route was therefore inapplicable to the synthesis of these compounds. By contrast with these findings, we have found the carbodi-imide method to be particularly useful for the synthesis of these derivatives. Thus tetra-*O*-acetyl-β-D-glucosamine (IV) was condensed with benzyloxycarbonylglycine and α-benzyl benzyloxycarbonyl-L-aspartate (V) to give the glucopeptide acetates (VIIIa) and (IIb) respectively in good yield.

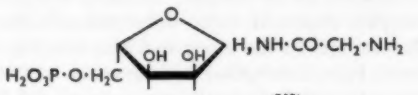
From the glucopeptide acetate (VIIIa) Bergmann and Zervas [17] removed *O*-acetyl groups with sodium methoxide and the benzyloxycarbonyl group by catalytic hydrogenation. Deacetylation with sodium methoxide was, however, inappropriate in the case of the glucopeptide acetate (IIb) since this reagent would be expected to cause transesterification with the formation of an α-methyl ester (IIc). In an attempt to effect simultaneous

[12] Bryant, Moore, Pimlott, and Young, *J.*, 1959, 3868.
[13] Busch, Hurlbert, and Potter, *J. Biol. Chem.*, 1952, **196**, 717.
[14] Sheehan and Hess, *J. Amer. Chem. Soc.*, 1955, **77**, 1067.
[15] Cohn and Edsall, "Proteins, Amino Acids and Peptides," Reinhold Publ. Corp., New York, 1943 p. 84.
[16] Moore and Stein, *J. Biol. Chem.*, 1948, **176**, 367.
[17] Bergmann and Zervas, *Ber.*, 1932, **65**, 1201.
[18] Doherty, Popenoe, and Link, *J. Amer. Chem. Soc.*, 1953, **75**, 3466; Popenoe, Doherty, and Link *J. Amer. Chem. Soc.*, 1953, **75**, 3469.
[19] Bergmann and Zervas, *Ber.*, 1932, **65**, 1192.

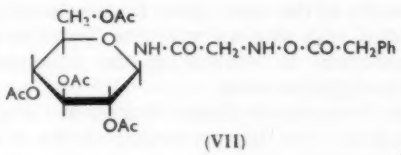
deacetylation and hydrolysis of the benzyl ester group, the glucopeptide acetate (IIb) was treated with lithium hydroxide in aqueous acetone, and after removal of the excess of lithium ions by passage through Zeo-Karb 225 resin (H^+ form) an oil was obtained. This oil was catalytically hydrogenated. The product, thought to be the glucopeptide (IIa), which could not be crystallized, was hydrolysed with N-hydrochloric acid for 2·5 hr., and



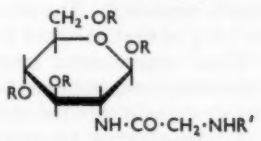
(V)



(VI)



(VII)



(VIIIa: R = Ac; R′ = O·CO·CH_2Ph)

(VIIIb: R = R′ = H)

the hydrolysate shown by paper chromatography to contain aspartic acid in the expected amount but only a trace of glucosamine. This suggested that dehydration of the glucosamine moiety had occurred since it is known that under the alkaline conditions of the Morgan–Elson procedure (0·05N-sodium carbonate, 100° for 4 min.), *N*-acetylglucosamine is converted into anhydro-chromogenic derivatives.[20] This idea received support from the observation reported in the review by Baer[21] that treatment of penta-acetylglucosamine with barium methoxide or barium hydroxide in cold methanol results in rapid dehydration of approximately half of the compound with the formation of chromogens. To test this possibility the product of alkaline deacetylation and hydrogenation of the glucopeptide acetate (IIb) was treated with Ehrlich reagent. The consequent production of an intense magenta colour confirmed that dehydration of the glucosamine moiety had occurred with the formation of chromogens. These results probably explain the failure of Doherty *et al.*[18] to obtain crystalline products on alkaline deacetylation of *O*-acetyl derivatives of *N*-acylglucosamines, and show that such compounds should not be exposed to alkaline conditions.

Conditions of acid hydrolysis were then sought which would result in de-*O*-acetylation of the glucopeptide acetate (IIb) without removal of the *N*-acyl group. The hydrolysis of α-glucosamine penta-acetate by 2·5N-sulphuric acid at room temperature was followed polarimetrically; after 36 hr. the specific rotation became constant and equal to that of *N*-acetylglucosamine. After neutralisation of the solution with barium hydroxide and removal of the barium sulphate, the supernatant liquid was shown by paper chromatography to contain *N*-acetylglucosamine together with traces of glucosamine. The residue obtained on evaporation was purified by several crystallisations and shown to be *N*-acetylglucosamine. Accordingly, after removal of the benzyloxycarbonyl and benzyl groups by catalytic hydrogenation, the product (IId) was treated with 2·5N-sulphuric acid at room temperature for 44 hr., and after neutralization *N*-(L-β-aspartyl)-D-glucosamine (IIa) isolated.* It was of interest that when the latter product was heated with the ninhydrin reagent of Moore and Stein[16] a brown colour was obtained identical with that obtained with asparagine. The pK_2 value of 8·82 found for the glucopeptide (IIa) was in close agreement with the pK_2 value of 8·80 found for the α-amino-group of asparagine.[15]

* In a recent brief communication Rothfus[5] reports the preparation of the glucopeptide (IIa); no details are given, however, of the method of preparation, or of the properties of this compound.

[20] Kuhn and Krüger, *Chem. Ber.*, 1956, **89**, 1473; 1957, **90**, 264.
[21] Baer, *Fortschr. Chem. Forsch.*, 1958, **3**, 830.

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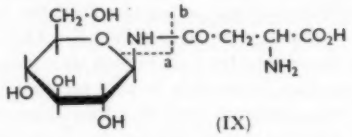
It has been previously observed [21] that *N*-acyl derivatives of glucosamine, in which the *N*-acyl group is represented by an amino-acid residue, give a positive Morgan–Elson reaction. In accordance with this the glucopeptide (IIa) gave a positive Morgan–Elson test, the coloured complex with *p*-dimethylaminobenzaldehyde showing light absorption with maxima at 538 and 576 mμ, and requiring >4 hr. for the maximum intensity of absorption to be reached at room temperature. These characteristics of the coloured complex enable it to be differentiated from the coloured complex formed by *N*-acetylglucosamine in the Morgan–Elson reaction since in the latter case the coloured complex shows light absorption with maxima at 550 and 590 mμ and the maximum intensity of absorption of both peaks was reached 1·5 hr. after the addition of the *p*-dimethylaminobenzaldehyde reagent.[22] The maximum intensity of the colour given by the glucopeptide (IIa) was 7·5% of that obtained by Aminoff *et al.* with an equal weight of *N*-acetylglucosamine. These observations may be of assistance in establishing the structures of glucopeptide fragments obtained by hydrolysis of glycoproteins.

In further experiments the stability of the *N*-acylglucosylamine linkage in the glucopeptide (Ia) to alkaline treatment was studied. For the conversion of the *N*-acylglucosylamine (Ia) to a nitrogen-free monosaccharide, ammonia, and aspartic acid, two bonds are required to be cleaved, *viz.*, the glucosylamine and the amide bond. It was most convenient to follow the hydrolysis of this compound by measuring the release of ammonia, bearing in mind that the formation of the latter is the result of two consecutive reactions, *i.e.*, fission of bond a or b (see IX) and subsequent hydrolysis of the glucosyl-



(IX)

amine or the asparagine formed. The compound was dissolved in 0·2N-sodium hydroxide and a stream of nitrogen gas passed through the boiling solution to drive the ammonia liberated into a 2% boric acid solution which was titrated at intervals with standard acid. The rate of liberation of ammonia followed first-order kinetics and gave a rate constant of $5{\cdot}5 \times 10^{-3}$ min.$^{-1}$ at 100°. In 0·5N-sodium hydroxide at room temperature the linkage was found by optical-rotation measurement to be stable for 7 hr.

In order to rupture the postulated *N*-acylglucosylamine link in egg albumin and thus separate carbohydrate from peptide, the fission of either bond a or b (see IX) would suffice. From this point of view it was important to know how the rate of liberation of ammonia from the *N*-acylglucosylamine linkage compared with that from the carbon–nitrogen link in both asparagine and glucosylamine, since it was possible that a rapid fission of either link a or b was followed by slow hydrolysis of glucosylamine or asparagine. In such a case conditions milder than those required for the release of ammonia from the *N*-acylglucosylamine link might suffice for the cleavage of either the a or b link. Accordingly, the liberation of ammonia from D-(+)-glucosylamine and L-(+)-asparagine in 0·2N-sodium hydroxide at 100° was measured by the method used for the glucopeptide (Ia) and the rate of liberation of ammonia found to follow first-order kinetics in both cases. A rate constant of $42{\cdot}2 \times 10^{-3}$ min.$^{-1}$ was found for the former compound and $14{\cdot}5 \times 10^{-3}$ min.$^{-1}$ for the latter under these conditions of hydrolysis. These results reveal that the carbon–nitrogen bonds in D-(+)-glucosylamine and L-(+)-asparagine are cleaved considerably more readily than are either of the two carbon–nitrogen bonds (*a*, *b*) in the *N*-acylglucosylamine linkage. Similar findings were obtained with *N*-acetyl-D-glucosylamine, prepared by the method of Brigl and Keppler.[23] The first-order rate constant for the liberation of ammonia from this

[21] Aminoff, Morgan, and Watkins, *Biochem. J.*, 1952, **51**, 379.
[23] Brigl and Keppler, *Z. physiol. Chem.*, 1929, **180**, 38.

linkage by 0·2N-sodium hydroxide at 100° was $2·7 \times 10^{-3}$ min.$^{-1}$ compared with $41·0 \times 10^{-3}$ and $42·2 \times 10^{-3}$ min.$^{-1}$ found for acetamide and D-(+)-glucosylamine respectively under the same conditions. These results rule out the possibility of rapid fission of either link *a* or *b* of the *N*-acylglucosylamine followed by slow hydrolysis of glucosylamine or asparagine.

The stability to acid of the *N*-acylglucosylamine linkage in the glucopeptide (Ia) was next studied. After treatment with N-hydrochloric acid at 100° for 2 hr. the compound was found by paper chromatography to be partially hydrolysed to aspartic acid and glucose. It was most convenient to follow this hydrolysis by measuring the release of glucose by Hoffman's method,[24] adapted for the "Autoanalyser," bearing in mind that we were only measuring the fission of bond *a*. The rate of liberation of glucose followed first-order kinetics and gave a rate constant $4·9 \times 10^{-3}$ min.$^{-1}$ at 100° in N-hydrochloric acid, similar to the value ($7·8 \times 10^{-3}$ min.$^{-1}$) found for the liberation of glucose, under the same conditions of hydrolysis from *N*-glycyl-β-D-glucosylamine hydrogen oxalate (kindly made available to us by Professor J. Baddiley, F.R.S.).

Since our measurement of the extent of acid hydrolysis of this compound was confined to the measurement of the fission of bond *a*, it was possible that a rapid fission of link *b* is followed by a slow cleavage of the liberated glucosylamine. This is unlikely for two reasons: (*a*) *NN*-dimethylglucosylamine is very rapidly hydrolysed by acid;[25] (*b*) milder conditions of acid hydrolysis used by Baddiley *et al.*,[8] *viz.*, 0·1N-hydrochloric acid at 100° for 4 hr., were without effect on *N*-glycyl-β-D-glucosylamine hydrogen oxalate.

It is of considerable interest that hydrolysis of the *N*-acylglucosylamine linkage in the glucopeptide (Ia) proceeds with approximately the same speed in 0·2N-sodium hydroxide as in N-hydrochloric acid. That hydrolysis is considerably more rapid in alkali than in acid of equivalent strength is a characteristic of amide hydrolysis[26] and suggests that fission of the amide link b is the rate-determining step in both acid and alkaline hydrolysis, followed by a rapid hydrolysis of the glucosylamine linkage a. This idea is supported for the case of acid hydrolysis by the following considerations. Isbell and Frush[27] have studied the mechanism of hydrolysis of L-arabinosylamine and have concluded that the iminium ion, $>C=NH_2^+$, formed by rupture of the ring after addition of a proton to the ring oxygen is a key intermediate. However, resonance in the amide structure of the *N*-acylglycosylamines will result in partial sharing of the lone pair of electrons of the nitrogen atom with the adjacent oxygen-bearing carbon atom. The resultant fractional positive charge on the nitrogen atom would inhibit the formation of the iminium ion, and hydrolysis of the glucosylamine bond would be suppressed. This is in accord with the view that fission of the amide linkage b is the rate-determining step in the hydrolysis of the *N*-acylglucosylamine linkage.

The stability of the amide linkage in the glucopeptide (IIa) to acid hydrolysis was the next subject of study. It was most convenient to follow this hydrolysis by means of the Morgan–Elson reaction. The rate of hydrolysis followed first-order kinetics and gave a rate constant $3·4 \times 10^{-3}$ min.$^{-1}$ at 100° in N-hydrochloric acid, similar to the first-order rate constant of $4·9 \times 10^{-3}$ min.$^{-1}$ for hydrolysis of *N*-(L-β-aspartyl)-β-D-glucosylamine (Ia) in the same conditions.

Experimental

Potentiometric Titration.—Solutions (1 ml.) of the glucopeptides (Ia) and (IIa) in 0·1N-potassium chloride were titrated. The pH was varied from 2·5 to 11 by using hydrochloric acid and sodium hydroxide of 0·2N-concentration in 0·1N-potassium chloride. A microglass

[24] Hoffman, *J. Biol. Chem.*, 1937, **120**, 51.
[25] Kenner, in "Ciba Foundation Symposium on Chemistry and Biology of Purines," ed. Wolstenholme and Millar, Churchill Ltd., London, 1957, p. 312.
[26] Taylor and Baker, "Sidgwick's Organic Chemistry of Nitrogen," Oxford University Press, 1945, p. 145.
[27] Isbell and Frush, *J. Res. Nat. Bur. Stand.*, 1951, **46**, 132.

electrode was used in conjunction with a potassium chloride salt bridge. Appropriate corrections were made by adding acid or alkali to volumes of 0·1N-potassium chloride similar to those used in the experiments. From the end-points equivalent weights and p*K* values were determined.

α-Benzyl Benzyloxycarbonyl-L-aspartate.—Benzyloxycarbonyl-L-aspartic anhydride (8·5 g.) and benzyl alcohol (5·4 g.) were heated in a sealed tube at 100° for 4 hr. The resulting syrup was dissolved in ether and extracted with successive portions of aqueous sodium carbonate; the later fractions crystallized on acidification, to give α-benzyl benzyloxycarbonyl-L-aspartate which recrystallised from ethyl acetate–light petroleum, then having m. p. 84—85° (2·5 g.), $[\alpha]_D^{23}$ −14·2° (*c* 2·5 in acetone). Bergmann, Zervas, and Salzmann [10] record m. p. 84—85°; Bryant *et al.*[12] record $[\alpha]_D^{17}$ −14·8° (*c* 5·0 in acetone). The earlier fractions were combined and additional quantities of the pure α-benzyl ester were obtained by repetition of the extraction procedure.

2,3,4,6-*Tetra*-O-*acetyl*-N-(α-*benzyl Benzyloxycarbonyl*-L-β-*aspartyl*)-β-D-*glucopyranosylamine*.—Dicyclohexylcarbodi-imide (0·27 g.) was added to a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (0·43 g.; obtained by reduction of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide [28]) and α-benzyl benzyloxycarbonyl-L-aspartate (0·45 g.) in dry methylene chloride (15 ml.). The solution was stirred for 6 hr. at room temperature, a few drops of glacial acetic acid were added (to decompose unchanged di-imide), and stirring was continued for a further ½ hr. Dicyclohexylurea, which had separated, was filtered off and the solvent was removed under reduced pressure. The residue was extracted into ethyl acetate, and washed successively with N-hydrochloric acid, water, aqueous sodium hydrogen carbonate, and water. After drying (Na_2SO_4), the solvent was removed under reduced pressure, and, after recrystallization of the residue from absolute ethanol, the product (0·56 g., 66%) had m. p. 139—141°. One further recrystallization afforded the *glucopeptide acetate* as needles, m. p. 142·5—143·5°, $[\alpha]_D^{23}$ +19·0° (*c* 2·01 in $CHCl_3$) (Found: C, 58·1; H, 5·4; N, 4·1. $C_{33}H_{38}N_2O_{14}$ requires C, 57·7; H, 5·6; N, 4·1%).

N-(*Benzyloxycarbonyl*-L-β-*aspartyl*)-β-D-*glucopyranosylamine*.—2,3,4,6-Tetra-*O*-acetyl-*N*-(α-benzyl benzyloxycarbonyl-L-β-aspartyl)-β-D-glucopyranosylamine (0·69 g.) was dissolved in aqueous acetone (1 : 4, 100 ml.), and a solution of lithium hydroxide (0·13 g.) in water (8 ml.) was added during ¾ hr. with stirring at room temperature. After being kept at 4° for 2 hr. the solution was concentrated to 40 ml. under reduced pressure at room temperature, and then after addition of water (60 ml.) was passed slowly through a column of Zeo-Karb 225 resin (H^+ form; 2 × 9 cm.). The column was washed with water until the effluent had a negative Molisch reaction, and the combined effluents were evaporated to 2 ml. On addition of methanol (25 ml.) and cooling overnight, needles separated, having m. p. 125—130° (0·20 g.), and the mother liquors yielded a further 0·04 g., m. p. 120—125° (total yield, 54%). Recrystallization from methanol afforded the *product*, m. p. 125—130°, $[\alpha]_D^{20}$ −8·3° (*c* 0·603 in H_2O) (Found: N, 6·3; equiv., 446. $C_{18}H_{24}N_2O_{10},H_2O$ requires N, 6·3%; equiv., 446).

N-(L-β-*Aspartyl*)-β-D-*glucopyranosylamine*.—*N*-(Benzyloxycarbonyl-L-β-aspartyl)-β-D-glucopyranosylamine (0·086 g.) was hydrogenolysed in water (25 ml.) with 8% palladized charcoal. Evolution of carbon dioxide had ceased after 1 hr. and the solution was then filtered from the catalyst, which was washed with water. The combined solution and washings were concentrated to 1 ml., and methanol (20 ml.) was added, whereupon the product, m. p. 200—203° (decomp.) (58 mg., 84%), separated. Two further recrystallizations from water–methanol afforded the hydrated *glucopeptide*, m. p. 203—204° (decomp.), $[\alpha]_D^{20}$ −17·3° (*c* 0·55 in H_2O), pK_2 8·82 (Found: C, 39·6; H, 6·4; N, 9·0. $C_{10}H_{18}N_2O_8,\frac{1}{2}H_2O$ requires C, 39·6; H, 6·3; N, 9·2%). Very recently Coutsogeorgopoulos and Zervas [29] reported the preparation of the glucopeptide (Ia) by a novel route. They record $[\alpha]_D^{16}$ −16·5° (in H_2O) and m. p. 253° (decomp.) for their glucopeptide (obtained as the anhydrous form). While their specific rotation is in agreement with our value, their m. p. is higher than that found for our glucopeptide (obtained as the hemihydrate). We therefore recrystallized our glucopeptide according to their directions and after drying the compound at 105° for 4 hr. obtained the anhydrous form (Found: C, 40·4; H, 6·5; N, 9·4. Calc. for $C_{10}H_{18}N_2O_8$: C, 40·8; H, 6·2; N, 9·5%). The melting behaviour was examined on a Kofler micro heating stage in polarized light; the material did not melt sharply but sintered at 208° and birefringence disappeared completely at 240°.

[28] Berthoe and Maier, *Annalen*, 1932, **498**, 50.
[29] Coutsogeorgopoulos and Zervas, *J. Amer. Chem. Soc.*, 1961, **83**, 1885.

1,3,4,6-*Tetra*-O-*acetyl*-N-(*benzyloxycarbonylglycyl*)-β-D-*glucosamine*.—Dicyclohexylcarbodiimide (0·45 g.) was added to a solution of benzyloxycarbonylglycine (0·41 g.) and 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine (0·67 g.) in dry methylene chloride (45 ml.), and the reaction carried out as described above. Crystallization of the crude product from ethanol afforded needles, m. p. 166—168° (0·75 g., 72%). Bergmann and Zervas [17] record m. p. 165°.

1,3,4,6-*Tetra*-O-*acetyl*-N-(α-*benzyl Benzyloxycarbonyl*-L-β-*aspartyl*)-β-D-*glucosamine*.—Dicyclohexylcarbodi-imide (0·29 g.) was added to a solution of 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine (0·44 g.) and α-benzyl benzyloxycarbonyl-L-aspartate (0·45 g.) in dry methylene chloride (15 ml.) and the reaction carried out as described above. Crystallization of the crude product from ethanol gave needles of m. p. 208—209° (0·65 g., 76%). After recrystallization from ethanol the *glucopeptide acetate* had m. p. 209·5—210·5°, $[\alpha]_D^{22}$ +6·3° (*c* 1·27 in acetone) (Found: C, 57·7; H, 5·4; N, 4·0. $C_{32}H_{38}N_2O_{14}$ requires C, 57·7; H, 5·6; N, 4·1%).

N-(L-β-*Aspartyl*)-D-*glucosamine*.—1,3,4,6-Tetra-*O*-acetyl-*N*-(α-benzyl benzyloxycarbonyl-L-β-aspartyl)-β-D-glucosamine (0·62 g.) was hydrogenolysed in glacial acetic acid (30 ml.) with 8% palladized charcoal. Evolution of carbon dioxide had ceased after 22 hr. and the solution was then filtered from the catalyst, which was washed with acetic acid. After evaporation of the solvent (the last traces *in vacuo* over potassium hydroxide), the residue was triturated with methanol–ether (1 : 1), whereupon crystals separated (0·33 g., 79%). Without further purification, this product (0·23 g.) was dissolved in 2·5N-sulphuric acid (10 ml.), and the hydrolysis followed polarimetrically at room temperature. After 44 hr. the solution was brought to pH 4 by the addition of saturated barium hydroxide and, after removal of the barium sulphate by centrifugation, the solution was evaporated to dryness under reduced pressure. The solid residue was dissolved in water (5 ml.); on addition of methanol (30 ml.) and cooling, crystals separated (0·125 g., 87%). After three recrystallizations from water–methanol the *glucopeptide* had m. p. >260° after darkening from 200°, $[\alpha]_D$ +29° ⟶ +22° (*c* 0·28 in H_2O), pK_2 8·82 (Found: C, 37·6; H, 6·3; N, 8·4; equiv., 318. $C_{10}H_{16}N_2O_8,1\frac{1}{2}H_2O$ requires C, 37·4; H, 6·6; N, 8·7%; equiv., 321).

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959. *The Preparation and Properties of Disilylcyanamide.*

By E. A. V. EBSWORTH and M. J. MAYS.

Disilylcyanamide, $(SiH_3)_2N{\cdot}CN$, has been obtained by interaction of silver cyanamide and bromo- or iodo-silane, and some of its physical properties have been determined. The silicon–nitrogen bonds are broken almost quantitatively by hydrogen chloride; an unstable addition compound is formed with boron trifluoride. The reactions with certain silver salts have also been investigated.

IODOSILANE reacts with a number of salts of silver, mercury(II) and lead(II) to give the iodide of the heavy metal and the silyl derivative of the anion; [1] we have prepared disilylcyanamide, $(SiH_3)_2N{\cdot}CN$, from silver cyanamide and iodosilane: $2SiH_3I + Ag_2N{\cdot}CN = (SiH_3)_2N{\cdot}CN + 2AgI$. Iodosilane vapour is allowed to pass over a mixture of silver cyanamide and glass wool, initially at room temperature: yields are never greater than 25% and are often less, but attempts to improve them by varying the conditions of the reaction have so far proved unsuccessful. Since it has been shown that disilylcyanamide decomposes in the presence of silver cyanamide, the low yields are perhaps not surprising.

Disilylcyanamide is a colourless liquid which is stable at room temperature for days in sealed apparatus, but decomposes slightly if heated to about 80° for some hours. Its Trouton constant shows that there is little association in the liquid phase. The infrared

[1] Emeléus, MacDiarmid, and Maddock, *J. Inorg. Nuclear Chem.*, 1955, **1**, 194; MacDiarmid, *ibid.*, 1955, **2**, 88; Downs and Ebsworth, *J.*, 1960, 3516.

spectrum has been recorded, but no vibrational assignments have yet been made—these are under study. The nuclear magnetic resonance shows chemical shifts of the protons very close to those obtained for trisilylamine, *N*-methylsilylamines, and silyl isothiocyanate, suggesting that this parameter is largely determined by the nature of the other atom bound to silicon; the ^{29}SiH coupling constant is closer to the values obtained for disiloxane and disilyl sulphide (see Table).

Nuclear magnetic resonance couplings and SiH chemical shifts in disilylcyanamide and related compounds.

	τ ($\pm$0·01)	$J_{^{29}SiH}$		τ ($\pm$0·01)	$J_{^{29}SiH}$
$(SiH_3)_2N{\cdot}CN$	5·55	225 $\pm$ 1	$SiH_3{\cdot}NCS$ [b]	5·55	240 $\pm$ 2
$(SiH_3)_2N$ [a]	5·56	212 $\pm$ 2	$(SiH_3)_2O$ [b]	5·39	221·5 $\pm$ 0·2
$(SiH_3)_2N{\cdot}CH_3$ [a]	5·56	212 $\pm$ 2	$(SiH_3)_2S$ [b]	5·66	224·0 $\pm$ 0·3
$SiH_3{\cdot}N(CH_3)_2$ [a]	5·66 ($\pm$0·04)	208 $\pm$ 2			

[a] Ebsworth and Sheppard, *J. Inorg. Nuclear Chem.*, 1959, **9**, 95. [b] Ebsworth and Turner, unpublished work.

None of the physical properties so far studied indicates whether the compound has the structure $(SiH_3)_2N{\cdot}CN$, as so far assumed, or $SiH_3{\cdot}N{:}C{:}N{\cdot}SiH_3$, which is also possible in principle; the vibrational spectrum may help to decide this point.

The compound reacts with hydrogen chloride according to the equation $(SiH_3)_2N{\cdot}CN + 4HCl = 2SiH_3Cl + H_2N{\cdot}CCl_2{\cdot}NH_2$. It reacts with silver thiocyanate and with silver chloride at room temperature, forming the silyl derivative of the anion; though neither reaction is quantitative, none of the disilylcyanamide was recovered in either case. Unchanged disilylcyanamide, however, was recovered after passage over silver bromide, and no bromosilane was detected among the products of the reaction; in a subsequent experiment, bromosilane was found to react with silver cyanamide, to give disilylcyanamide, so it seems that cyanamide should be included in MacDiarmid's conversion series [2] between bromide and chloride.

The reaction between disilylcyanamide and boron trifluoride is complex. When an excess of boron trifluoride is kept with disilylcyanamide for 18 hours at $-78°$, the volatile products consist of a mixture of boron trifluoride and fluorosilane; analysis suggest that the combining ratio (BF_3 : cyanamide) approaches 2 : 1 at low temperatures. When the solid residue attains room temperature, more boron trifluoride and fluorosilane are evolved, leaving a white solid which when heated gives off fluorosilane but no boron trifluoride. These observations may be interpreted in terms of the following reactions:

$$(SiH_3)_2N{\cdot}CN + BF_3 \rightleftharpoons (SiH_3)_2N(BF_3){\cdot}CN \quad (1)$$

$$(SiH_3)_2N(BF_3){\cdot}CN \longrightarrow SiH_3F + SiH_3{\cdot}N(BF_2){\cdot}CN \quad (2)$$

$$SiH_3{\cdot}N(BF_2){\cdot}CN + BF_3 \rightleftharpoons [SiH_3{\cdot}N(BF_2){\cdot}CN]BF_3 \quad (3)$$

$$\downarrow \text{Heat}$$

$$SiH_3F + (BFCN_2) \quad (4)$$

About 80% of the silyl groups present initially in the disilylcyanamide are evolved as fluorosilane after 18 hours at $-78°$, showing that reaction (4) occurs slowly even at this low temperature. This complex reaction is in keeping with those of silylamines and silyl cyanides with boron trifluoride.[3]

Experimental

Preparation of Disilylcyanamide.—In a typical experiment, iodosilane (1·0 g.) was allowed to pass as vapour over a mixture of silver cyanamide (6 g.) and powdered glass wool (12 g.). The solid became grey-black and hot, while a little hydrogen was produced. From the volatile products *disilylcyanamide* (0·065 g.) was obtained (Found: SiH, 5·8; N, 27·4%; *M*, 102.

[2] MacDiarmid, *Quart. Rev.*, 1956, **10**, 208.

[3] Sujishi and Witz, *J. Amer. Chem. Soc.*, 1957, **79**, 2447; Ebsworth and Emeléus, *J.*, 1958, 2150; Evers, Freitag, Kriner, MacDiarmid, and Sujishi, *J. Inorg. Nuclear Chem.*, 1959, **13**, 239.

$CH_4N_2Si_2$ requires SiH, 5·9; N, 27·4%; *M*, 102). The other volatile products included silane, disiloxane, and hydrogen cyanide (identified spectroscopically and from molecular-weight measurements). In other experiments, disilylcyanamide was obtained from the reactions between iodosilane and lead(II) cyanamide, and from bromosilane and silver cyanamide, but the yield was 10—20% in each case; when iodosilane was allowed to react with undiluted silver cyanamide, the mixture exploded.

Physical properties of the product were determined for samples which had been repeatedly distilled at −46° and condensed at −64°. The compound melts at −74·8° ± 0·5°; the b. p. (extrapolated over 4° from a vapour-pressure curve) is 84·7° ± 0·5°, and the vapour pressures between 50° and the boiling point are given by the equation $\log_{10} p(\text{mm.}) = 7{\cdot}800 - 1761/T$. The vapour pressure at 0° is 18·5 mm.

The latent heat at the b. p. is 8100 ± 50 cal./mole^{-1} and Trouton's constant is 22·6. The vapour pressures obtained on cooling showed that there had been slight decomposition during the experiment.

The proton resonance spectrum of the compound dissolved in cyclohexane consisted of the expected single sharp peak, with satellites due to ^{29}SiH groups; the chemical shift τ in 10% solution measured relative to cyclohexane as solvent is 5·55 ± 0·01 p.p.m., and is unchanged for a 3% solution in the same solvent. The ^{29}SiH coupling constant is 225 ± 1 c/s. Strong infrared absorption bands appear at 2200, 950, 800, and 740 cm.$^{-1}$.

The compound was stable at room temperature in sealed apparatus for several days, but decomposed slightly during 3 hr. at 80°. The infrared spectrum of the decomposition products suggests that a trace of silane had been formed.

In the presence of solid silver cyanamide, decomposition is rapid and almost explosive at room temperature, being complete in a few minutes. The yellow silver salt becomes grey, and the volatile material recovered includes silane, hydrogen cyanide, and a non-condensable gas.

Reactions.—(a) *With hydrogen chloride.* Disilylcyanamide (0·0448 g.) and hydrogen chloride (0·0788 g.) were mixed and kept at −78° for 18 hr. The volatile products consisted of hydrogen chloride (0·0132 g.) (Found: *M*, 36·7; v. p. at −112°, 122 mm. Calc.: *M*, 36·5; v. p.[4] at −112°, 117 mm.) and chlorosilane (0·0613 g.) (Found: *M*, 66·6; v. p. at −64°, 131 cm. Calc.: *M*, 66·5; v. p.[5] at −64°, 137 mm.); an involatile white solid remained, soluble in water (Found, in a subsequent experiment: C, 10·7; H, 3·4; N, 24·4. Calc. for $CCl_2H_4N_2$: C, 10·5; H, 3·5; N, 24·4%); the aqueous solution was boiled with sodium hydroxide; and treatment with nitric acid and silver nitrate then gave 0·1256 g. of silver chloride. The molar ratio, cyanamide consumed : HCl consumed : SiH_3Cl formed : chloride in residue is 1·00 : 4·09 : 1·04 : 2·00.

(b) *With boron trifluoride.* Disilylcyanamide (0·33 mmole) was kept with boron trifluoride (1·78 mmoles) at −78° for 18 hr. The volatile material recovered at −96° (*M*, 63) was shown spectroscopically to be a mixture of boron trifluoride (*M*, 68) and fluorosilane (*M* 50); these compounds cannot be separated by distillation. A white solid residue evolved a mixture of boron trifluoride and fluorosilane when warmed to room temperature, and gave off fluorosilane alone when heated to 100° for 15 min.; 2·0 mmoles of volatile material were recovered in all. The solid residue left after heating was shown qualitatively to contain Si–H bonds (Found: C, 13·8; H, 1·8; N, 31·7. Calc. for $BFCN_2$: C, 17·1; N, 40·1%).

In a second experiment, disilylcyanamide (0·63 mmole) and boron trifluoride (2·63 mmole) were kept together at −78° for 18 hr.; 2·45 mmoles of volatile material were recovered at −96°, and when hydrolysed gave 3·32 mmoles of hydrogen. On the assumptions that all the Si–H bonds in the products were originally present as fluorosilane, and that no other volatile product was formed initially, the amount of boron trifluoride recovered is found by difference to be 1·29 mmoles, giving a molar combining ratio under the stated conditions of 1·86 : 1 [BF_3 : $(SiH_3)_2N{\cdot}CN$]. In a further experiment, disilylcyanamide (0·39 mmole) was kept with a 2 : 1 molar excess of boron trifluoride at −78° for 15 min.; a mixture of fluorosilane and boron trifluoride (1·66 mmoles) was recovered at −96°. When disilylcyanamide was kept with a large excess of boron trifluoride at −78° for 5 min., the volatile products recovered at −96° contained appreciable amounts of fluorosilane.

(c) *With silver chloride.* Disilylcyanamide (0·0175 g.) was allowed to pass as vapour over a 2 : 1 mixture of glass wool and silver chloride; chlorosilane was recovered (0·0078 g.) (Found:

[4] Giaque and Wiebe, *J. Amer. Chem. Soc.*, 1928, **50**, 101.
[5] Stock and Somieski, *Ber.*, 1919, **51**, 695.

M, 67; v. p. at −85°, 28 mm. Calc.: *M*, 66·5; v. p.[5] at −85°, 35 mm.); the identification was confirmed spectroscopically.

(d) *With silver thiocyanate.* When disilylcyanamide (0·016 g.) was allowed to pass as vapour over a 2 : 1 mixture of glass wool and silver thiocyanate, only 0·003 g. of volatile material was recovered. This had an infrared spectrum identical with that of silyl isothiocyanate, and when hydrolysed gave thiocyanate ion.

(e) *With silver bromide.* When disilylcyanamide (0·020 g.) was allowed to pass as vapour over a 2 : 1 mixture of powdered glass wool and silver bromide, volatile material was recovered [(0·014 g.) (v. p. at 0°, 31 mm. Calc. for SiH_3Br: v. p. at 0°, 710 mm.)]. The infrared spectrum showed that no bromosilane was present, and that the main component was disilylcyanamide. It was concluded that some decomposition of the starting material had occurred in the presence of the silver salt.

Starting Materials.—Iodosilane was prepared by treating silane with hydrogen iodide in the presence of aluminium iodide at 100°.[6] A solution of cyanamide was obtained from calcium cyanamide and sulphuric acid,[7] and on neutralization with quioklime and treatment with silver nitrate solution gave silver cyanamide.

We are grateful to Mr. S. Frankiss for help in recording the nuclear magnetic resonance spectra, to the Wellcome Foundation for lending the nuclear magnetic resonance spectrometer to the Department, and to the Department of Scientific and Industrial Research for a maintenance grant (to M. J. M.).

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The University, Cambridge. [*Received, May 18th*, 1961.]

[6] Emeléus, Maddock, and Reid, *J.*, 1941, 353.
[7] Nowak, *Przemysl Chem.*, 1957, **13**, 688; *Chem. Abs.*, 1958, **52**, 9625.

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960. *The Structure of Two Trimers of Biacetyl.*

By R. M. Cresswell, W. R. D. Smith, and H. C. S. Wood.

The preparation of a new trimer of biacetyl is described and, on the basis of its physical and chemical properties, structure (I) is suggested for this compound. The chemistry of a second trimer of biacetyl has been re-examined and a new structure (VII), based largely on physical evidence, is proposed.

We recently described [1] the condensation of a new trimer of biacetyl with 5-amino-4-D-ribitylaminouracil to give riboflavin and 6,7-dimethyl-8-D-ribityl-lumazine. We suggested that this reaction might be related to the biosynthesis of riboflavin and of the pteridine derivative. We now describe the preparation of this trimeric biacetyl and experiments which lead us to suggest structure (I) for this compound.

Biacetyl, when kept for 4—5 days at room temperature in contact with an anion-exchange resin (Amberlite CG-400, OH form), undergoes self-condensation; the crystalline product is the same as separates from some specimens of biacetyl which have been stored for long periods. Elementary analysis and molecular-weight determination indicate that the compound is a trimer, $C_{12}H_{18}O_6$. It differs, however, from that previously described.[2]

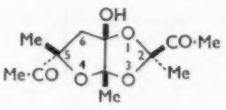
The infrared spectrum shows strong bands (in CCl_4) at 1724 (C=O) and 3460 cm.$^{-1}$ (OH). The nuclear magnetic resonance spectrum shows bands at 5·52 (hydroxyl proton), 7·741 and 7·804 (two different CH_3·CO), 8·608, 8·682, and 8·708 (three CH_3–C⩽O–), and two doublets at 6·87 and 8·24 τ (–CH_2–; AB type, J_{AB} = 13·5 cycles/sec.). The position of the hydroxyl band in these spectra indicates that there is relatively strong hydrogen bonding in the molecule, and as the position of this band in the infrared spectrum is not affected by dilution we conclude that the bonding is intramolecular. It is to be expected that there would also be two bands in the 6 μ region corresponding to bonded and unbonded

[1] Cresswell and Wood, *J.*, 1960, 4768.
[2] Diels and Jost, *Ber.*, 1902, **35**, 3290.

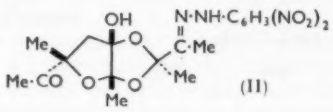
carbonyl groups; we have, however, been unable, even by using a calcium fluoride prism and slow scanning speeds, to split the single band at 1724 cm.$^{-1}$.

The trimer is very unstable and it has been possible to prepare only one derivative of the intact molecule. Treatment with an excess of 2,4-dinitrophenylhydrazine sulphate in methanol gave, almost immediately, a yellow monodinitrophenylhydrazone whose infrared spectrum (in Nujol) showed a strong band at 1709 cm.$^{-1}$ (C=O). The spectrum in the

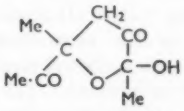
(I)



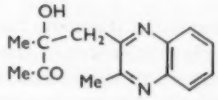
(II)



(III)



(IV)



2—4 μ region of a dilute solution in carbon tetrachloride (1 cm. cells) showed absorption characteristic of an unbonded hydroxyl group (3610 cm.$^{-1}$). This derivative recrystallised unchanged from nitrobenzene, but in a hydroxylic solvent such as ethanol hydrolysis gave the monodinitrophenylhydrazone of biacetyl as the only isolable product. We conclude that the original dinitrophenylhydrazone is best represented by structure (II), and that hydrolysis proceeds by successive breaking of acetal linkages to give the monodinitrophenylhydrazone of biacetyl and biacetyl dimer (III or the related open-chain hexanetrione). We have confirmed the presence of this dimer in the ethanolic mother liquors from the above recrystallisation by addition of a 4-alkylamino-5-aminouracil, obtaining pteridines analogous to those obtained in our previous work [1] and identified by paper chromatography.

Attempts to prepare other carbonyl or hydroxyl derivatives resulted in disruption, giving in most cases simple derivatives of biacetyl.

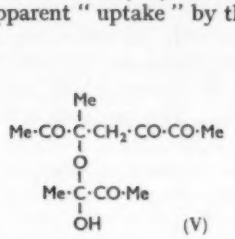
In aqueous solution of pH >8 the trimer behaves like a mixture of biacetyl and the aldol (III) (or the related open-chain hexanetrione). Thus, we have already reported [1] that it condenses with 4,5-diaminouracil, giving 6,7-dimethyl-lumazine and 2,4-dihydroxy-7-(2-hydroxy-2-methyl-3-oxobutyl)-6-methylpteridine. Similarly with *o*-phenylenediamine it gives 2,3-dimethyl- and 2-(2-hydroxy-2-methyl-3-oxobutyl)-3-methyl-quinoxaline (IV), the latter identical with a specimen prepared from the dimeric aldol (III) and *o*-phenylenediamine.

Structure (I) is derived from the dimer (III), the third molecule of biacetyl being attached by successive acetal linkages. There is, however, the possibility that the trimer is derived from an open-chain structure (V): successive ring closures involving acetal linkages could lead to structure (VI) or to two different bicyclo[3,2,1]systems. We have eliminated the last two possibilities because Dreiding models show that the distance between the hydroxyl group and either carbonyl group is too great to permit the hydrogen bonding indicated by the spectra. We have also eliminated structure (VI) which contains an α-hydroxy-ketone grouping since the trimer does not react with aqueous sodium periodate. This estimation was carried out by titration of the periodate in mineral acid solution with sodium thiosulphate and potassium iodide; [3] the standard technique [4] which involves titration with sodium arsenite in aqueous sodium hydrogen carbonate solution was not here feasible as at this pH the trimer dissociates rapidly (see above) into biacetyl

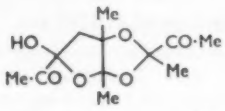
[3] Scott, "Standard Methods of Chemical Analysis," 5th Ed., Vol. I, van Nostrand, New York, 1939, p. 458.

[4] Jackson, *Organic Reactions*, Vol. 2, p. 361.

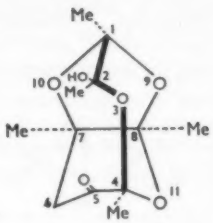
and the aldol (III), each of which then reacts with one equivalent of periodate giving an apparent " uptake " by the trimer molecule of two mol. of periodate.



(V)



(VI)



(VII)

The stereochemistry at positions 2 and 5 of the bicyclic ring system (I) must also be as shown for the following reason. The infrared spectrum of the monodinitrophenylhydrazone (II) shows no evidence of hydrogen bonding between carbonyl and hydroxyl groups, whereas in the trimer (I) strong hydrogen bonding is present. Therefore the carbonyl group attached at position 2 must be on the same side of the ring as the hydroxyl group, and that attached to position 5 must be on the opposite side. This configuration also explains why only one of the carbonyl groups reacts with dinitrophenylhydrazine, since the 5-acetyl group is sterically hindered by the 2-methyl group.

We have also re-examined the other trimer of biacetyl, first prepared by Diels and Jost [2] by treatment of biacetyl with concentrated hydrochloric acid at 0°. This compound shows infrared bands (CCl_4 solution) at 1727 (C=O) and 3610 cm.$^{-1}$ (unbonded OH). The nuclear magnetic resonance spectrum shows bands at 7·40 (hydroxyl proton), 8·45, 8·47, 8·59, 8·62, and 8·72 (five CH_3–C$\leqq$O–), and two doublets at 6·83 and 7·54 τ (–CH_2·CO– AB type, J_{AB} = 10·0 cycles/sec.). This evidence is incompatible with Diels and Jost's structure [2] and we suggest that this trimer has structure (VII). This is formed from the open-chain precursor (V) by successive acetal linkages. It is in agreement with Diels and Jost's report of monocarbonyl (oxime, semicarbazone etc.) and alcohol derivatives (monoacetate, phenylurethane). The stereochemistry at the carbon atom which carries the hydroxyl group is also defined, since the hydroxyl group must be remote from the carbonyl group to avoid hydrogen bonding. Structure (VII) is the only one which can accommodate the physical and chemical properties described above if we make the reasonable assumption that, in the formation from the precursor (V) of the *initial* acetal link, ring closure to give a 7-membered ring will not take place where formation of a 5-membered ring [which leads eventually to structure (VII)] or of a 6-membered ring (which leads to products which do not agree with the physical evidence) is possible.

Experimental

Infrared Spectra.—These were determined with a Grubb-Parsons spectrophotometer and sodium chloride and calcium fluoride prisms. The solvent was carbon tetrachloride in all cases except one indicated in the text.

Nuclear Magnetic Resonance Spectra.—The spectrum of compound (I) was determined with a Varian V-4300-2 spectrometer with a 40·0 Mc. oscillator. The spectrum, which was determined for a 6% solution in carbon tetrachloride, was calibrated by the side-band technique. The spectrum of compound (VII) was determined with a Varian A-60 spectrometer for a solution in deuterochloroform. Tetramethylsilane (1%) was added as an internal reference in each case.

Paper Chromatography.—Chromatograms were developed by the technique and solvent systems previously described.[1]

2,5-*Diacetyl*-3a,5,6,6a-*tetrahydro*-6a-*hydroxy*-2,3a,5-*trimethylfuro*[2,3-d]-1,3-*dioxole* (I).—An anion-exchange resin (Amberlite CG-400) was converted into its hydroxyl form by washing it with 5% sodium hydroxide solution. The resin was washed free from alkali with distilled water (carbonate-free), dried at 30°, and used within 24 hr.

The resin (10 g.) was added portionwise to biacetyl (30 c.c.) during 30 min., any rise in temperature being checked by external cooling. The mixture was kept for 5 days at room temperature with periodic mixing, a solid mass being obtained. Ether (100 c.c.) was added, the resin was removed by filtration, and the ether *in vacuo*. Water (3 c.c.) was added to the resulting pale yellow gum, which crystallised overnight at 0°. Recrystallisation from ether gave the *trimer* (7·5 g.) as colourless needles, m. p. 73—75° [Found: C, 55·9; H, 7·2%; *M* (ebullioscopic in C_6H_6), 251, 253. $(C_4H_6O_2)_3$ requires C, 55·8; H, 7·0%; *M*, 258]. *X*-Ray crystallography showed the crystal to be monoclinic and indicated that the unit cell contained 12 biacetyl units. This result also supports a trimeric structure.

The trimer (1 g.), dissolved in the minimum amount of methanol, was added to a solution of 2,4-dinitrophenylhydrazine (2·5 g.) and sulphuric acid (4 c.c.) in methanol (35 c.c.) and water (10 c.c.). A yellow precipitate was formed almost immediately, and after 10 min. was collected and recrystallised from nitrobenzene, to give the 2,4-*dinitrophenylhydrazone* (1·5 g.) as yellow needles, m. p. 155—156° (Found: C, 49·7; H, 4·9; N, 13·2. $C_{18}H_{22}N_4O_9$ requires C, 49·3; H, 5·1; N, 12·8%).

Attempted recrystallisation from ethanol gave biacetyl monodinitrophenylhydrazone [5] as orange needles, m. p. and mixed m. p. 174—175° (Found: C, 45·0; H, 3·6; N, 20·6. Calc. for $C_{10}H_{10}O_5N_4$: C, 45·1; H, 3·8; N, 21·0%), whose infrared spectrum was as reported.[5]

To the mother liquors from the ethanol recrystallisation was added a solution of 5-amino-4-2′-hydroxyethylaminouracil.[1] The mixture was heated on the steam bath for 15 min. and examined by paper chromatography. The mixture of pteridines obtained was identical with that formed [1] similarly from dimeric biacetyl (III).

2-(2-*Hydroxy*-2-*methyl*-3-*oxobutyl*)-3-*methylquinoxaline* (IV).—5-Acetyltetrahydro-2-hydroxy-2,5-dimethyl-3-oxofuran (III) (1·7 g.) in water (15 c.c.) was heated with *o*-phenylenediamine (1·08 g.) in water (10 c.c.) on the steam bath for 10 min. The pale yellow precipitate which separated on cooling recrystallised from aqueous ethanol, to give the *quinoxaline* (1·8 g.) as pale yellow needles, m. p. 110—112°. Sublimation at 110° (bath)/0·05 mm. gave colourless needles, m. p. 112—114° (Found: C, 68·6; H, 6·8; N, 11·3. $C_{14}H_{16}O_2N_2$ requires C, 68·8; H, 6·6; N, 11·5%).

Condensation of Trimeric Biacetyl (I) *with* o-*Phenylenediamine*.—Trimeric biacetyl (I) (0·6 g.) was heated with *o*-phenylenediamine (0·5 g.) in water (20 c.c.) on the steam bath for 5 min., then cooled and extracted with ether (3 × 50 c.c.). The extracts were dried (Na_2SO_4) and evaporated, giving a gum (0·85 g.) that was chromatographed in benzene on neutral alumina (Woelm; 25 g.). Benzene (200 c.c.) eluted a fraction (0·29 g.) which crystallised from aqueous ethanol, to give 6,7-dimethylquinoxaline,[6] m. p. and mixed m. p. 100—102°. Ether containing 1% of methanol (150 c.c.) eluted a second main fraction (0·32 g.) which crystallised from aqueous ethanol to give 2-(2-hydroxy-2-methyl-3-oxobutyl)-3-methylquinoxaline, m. p. 110—112°, identical with the material prepared as above.

Trimeric Biacetyl (2-*Hydroxy*-1,2,4,7,8-*pentamethyl*-3,9,10,11-*tetraoxotricyclo*[5,2,1,$1^{4,8}$]-*undecan*-5-*one*) (VII).—This compound was obtained by Diels and Jost's method [2] as colourless needles (from water), m. p. 102—103° (lit., 105°).

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[5] Reich and Hefle, *J. Org. Chem.*, 1956, **21**, 708.
[6] Bost and Towell, *J. Amer. Chem. Soc.*, 1948, **70**, 903.

961. *Complex Formation in Pyridine Solutions of Aromatic Polynitro-hydrocarbons.*

By R. E. Miller and W. F. K. Wynne-Jones.

Complex-formation in pyridine solutions of 1,3,5-trinitrobenzene has been studied in detail and equilibrium and kinetic data are presented. Two reactions occur, the first reversible and the second irreversible. Conductivity measurements show that both reactions lead to ionic species. The slow changes in similar systems involving 2,4,6-trinitrotoluene and 2,4,6-trinitro-*m*-xylene are also reported.

In a previous paper [1] we showed that *s*-trinitrobenzene dissolves in a number of aliphatic amines, giving at once solutions whose red colour is associated with an absorption band at 450—475 mμ. When *s*-trinitrobenzene is dissolved in pyridine a similar band is observed near 465 mμ, but the colour is formed slowly and is much less intense than that of diethylamine solutions containing the same trinitrobenzene concentration, which suggests that the equilibrium constant for the reaction is low. An additional absorption band near 570 mμ occurs only in solvents of relatively high dielectric constant.[1]

A slow secondary reaction producing an absorption band at about 514 mμ is also observed in solvents of high dielectric constant [1] though not in purified aliphatic amines.

Slow conductivity changes also occur in these solutions. Hantzsch and Caldwell [2] observed small electrical conductivities for pyridine solutions of *s*-trinitrobenzene and Davies [3] noted slow changes in electrical conductivity for which he found a unimolecular velocity constant.

The present paper describes the evaluation of kinetic and equilibrium results from light-absorption measurements that are correlated also with changes in electrical conductivity.

Experimental and Results

The apparatus used for the measurement of light absorption and that for determining electrical conductivity, and the purification of the nitro-compounds have been described elsewhere.[1]

In early measurements " AnalaR " pyridine for use as a solvent was refluxed over sodium hydroxide and distilled, the middle fraction being retained. Solutions of *s*-trinitrobenzene in pyridine purified by this method showed a marked induction period before development of colour. On further purification the induction period disappeared or become negligible.

The measurements recorded here have been obtained for " AnalaR " pyridine which had been refluxed for 3 hr. over barium oxide, then kept over this same oxide before being fractionated in a spinning-band column of high efficiency. The fraction of b. p. 114·0—114·4° was collected, stored in a flask fitted with soda-lime guard-tubes, and kept in the dark. When this pyridine was left for some months before use the induction period reappeared, perhaps owing to an impurity formed by the action of light or oxygen.

A few measurements were carried out in the absence of oxygen. Pyridine was distilled on to the solute in a vacuum, and nitrogen purified by passage through columns of silica gel, soda-lime, and active copper was allowed to enter the apparatus. After 90 min. the spectrum was measured and a second sample was analysed after about 3½ hr.

Results.—The spectrum of a typical solution at various times after mixing is shown in Fig. 1, and the variation with time of the optical density at the three maxima in Fig. 2a. The bands at 465 and 570 mμ follow one another closely and the ratio D_{570}/D_{479} remains constant except for an overlap effect produced by building-up of the product of the secondary reaction.

Curves for the variation with time of the " true " optical density, D', are shown in Fig. 2b. By the " true " optical density we mean that portion of the observed optical density due to the

[1] Miller and Wynne-Jones, *J.*, 1959, 2375.
[2] Hantzsch and Caldwell, *Z. phys. Chem.*, 1908, **61**, 228.
[3] Davies, *Trans. Faraday Soc.*, 1935, **31**, 1561.

species having its absorption maximum at the wavelength under consideration. This is smaller than the measured value by an overlap correction which can be estimated.

It is assumed that

$$D_{465} = D'_{470} + aD'_{514} \ (a \approx 0{\cdot}1), \quad (1)$$

and

$$D_{514} = D'_{514} + bD_{465} \ (b \approx 0{\cdot}31), \quad (2)$$

where D refers to the observed optical density and a and b are constants. These assumptions are not strictly valid but the errors introduced are small.

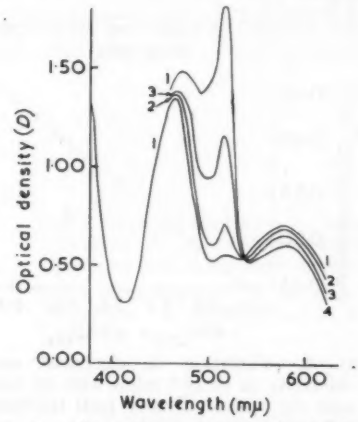

FIG. 1. Absorption spectrum of a typical solution (0·31M) of 1,3,5-trinitrobenzene in pyridine (cell thickness 0·5 cm.).

Times after mixing: (1) 25—45 min. (2) 50—69 min. (3) 140—168 min. (4) 294—316 min.

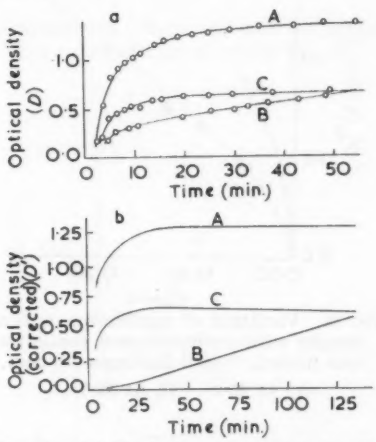

FIG. 2. (a) Variation of optical density with time for a typical solution (0·019M) of 1,3,5-trinitrobenzene in pyridine. (b) The same after correction for overlap.

A, 470 mμ. B, 514 mμ. C, 570 mμ.

Estimates of a and b are obtained by resolving spectra such as those in Fig. 1 into three separate bands above 400 mμ. The two bands having peaks at 470 mμ and 570 mμ are assumed to be symmetrical about their peak frequency; the third is obtained by difference. Fig. 2b indicates the occurrence of two consecutive reactions. Most measurements on the primary reaction have been made at 570 mμ where overlap corrections could be neglected.

To interpret the data for the primary reaction it is convenient to separate the effects of the two reactions. The observed value of D_{570} will be lower than if no secondary reaction had occurred as the latter involves destruction of the primary product. The value of the optical density D'' which would have been observed if no secondary reaction had occurred can be estimated. This is larger than the observed value D by an amount ΔD. It was found that $\mathrm{d}\Delta D_{570}/\mathrm{d}t = k'D_{570}$, so that $\Delta D_{570} = k'\int D_{570} \cdot \mathrm{d}t$. The correction can thus be obtained from a knowledge of k' and the area under the D_{570}–t curve. It is small and its effect is to hold D'' steady after the observed value begins to drop. These steady values of D'' ($D''_{\mathrm{eq.}}$) are plotted against *s*-trinitrobenzene concentration in Fig. 3. The curves of D'' against t are used to obtain kinetic data.

Measurements of the slope of curves such as B in Fig. 2b give the rate of formation of the secondary product. This is found to be proportional to D_{570}. The measurements carried out in an atmosphere of purified nitrogen indicated that the secondary reaction proceeded in the absence of oxygen.

Curves of specific conductivity against time initially resemble curves A and C of Fig. 2b: instead of reaching a maximum they continue to rise in a roughly linear manner, and the measurements indicate that both primary and secondary products are ionic. The relation

$$\kappa = A'D_{570} + B'D_{514} \quad (3)$$

is obeyed over a considerable range of time for a given solution: a typical conductivity curve is shown in Fig. 4a and is correlated with light absorption measurements in Fig. 4b. The

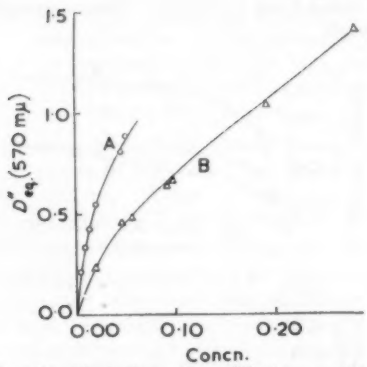

FIG. 3. Variation of equilibrium optical density with trinitrobenzene concentration (mole $l.^{-1}$) (cell thickness 0·5 cm.).

A, At 25·0°. B, At 39·7°.

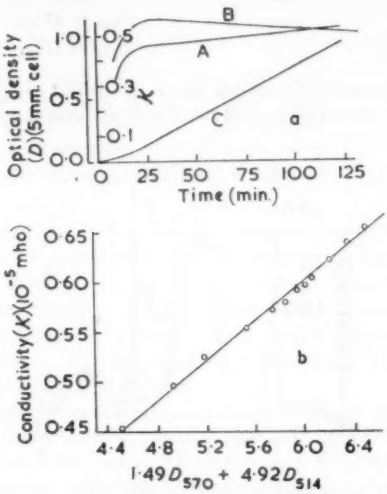

FIG. 4. Variation of electrical conductivity (κ in 10^{-5} mho) with (a) time and (b) optical density (cell thickness 0·5 cm.).

A, Conductivity. B, Optical density at 570 mμ. C, Optical density at 514 mμ.

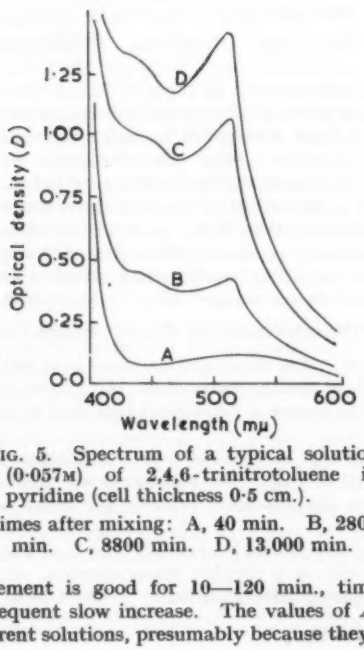

FIG. 5. Spectrum of a typical solution (0·057M) of 2,4,6-trinitrotoluene in pyridine (cell thickness 0·5 cm.).

Times after mixing: A, 40 min. B, 2800 min. C, 8800 min. D, 13,000 min.

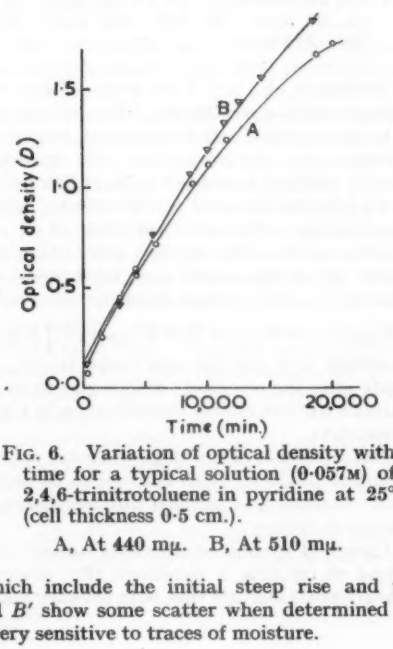

FIG. 6. Variation of optical density with time for a typical solution (0·057M) of 2,4,6-trinitrotoluene in pyridine at 25° (cell thickness 0·5 cm.).

A, At 440 mμ. B, At 510 mμ.

agreement is good for 10—120 min., times which include the initial steep rise and the subsequent slow increase. The values of A' and B' show some scatter when determined for different solutions, presumably because they are very sensitive to traces of moisture.

Pyridine solutions of 2,4,6-trinitrotoluene also show slow changes in conductivity and light absorption. Typical spectra are presented in Fig. 5. These solutions show a small initial conductivity κ_0 which varies with the square root of the concentration (c, in moles $l.^{-1}$) of the solute:

$$K_0 - K_{py} = 331 \times 10^{-3}c^{\frac{1}{2}} \text{ (at 25°)}, \quad (4)$$

where K_{py} is the specific conductivity of the solvent. Plots of optical density against time become almost linear after the first 800 min., the relation

$$dD_{510}/dt = 33{\cdot}2 \times 10^{-3}c^{\frac{1}{2}} \quad (5)$$

being then obeyed at 25°. Changes in light absorption have been followed for periods of several weeks without attainment of equilibrium. Typical results are shown in Fig. 6.

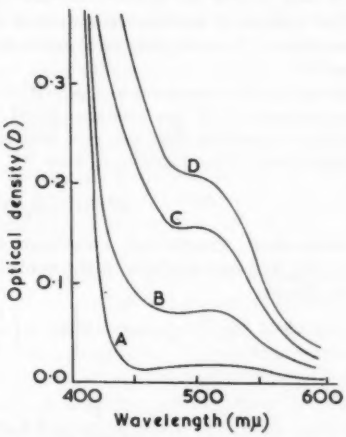

FIG. 7. Spectrum of a typical solution (0·049M) of 2,4,6-trinitro-*m*-xylene in pyridine (cell thickness 0·5 cm.).

Times after mixing: A, 30 min. B, 5500 min. C, 16,000 min. D, 26,000 min.

Pyridine solutions of 2,4,6-trinitro-*m*-xylene also show slow changes in conductivity and light absorption (see Fig. 7). Conductivity measurements for this system were not extensive but changes in light absorption were best fitted by the following relations at 25°:

$$10^4 dD_{510}/dt = 4{\cdot}05c^{\frac{1}{2}} - 0{\cdot}14 \quad (6)$$

and

$$10^4 dD_{440}/dt = 3{\cdot}43c + 0{\cdot}005. \quad (7)$$

Treatment of Results.—Measurements in benzene or ethanol show that *s*-trinitrobenzene forms a 1 : 1 complex with many amines or aromatic hydrocarbons and that the optical density at the wavelength at which the new band appears is directly proportional to the concentration of complex.[1] In the present case one of the reactants is the solvent and there seems good reason to suppose that only a small equilibrium concentration of primary product is formed. If a 1 : 1 complex were formed we should therefore expect $D''_{eq.}$ to be directly proportional to the initial *s*-trinitrobenzene concentration. Fig. 3 shows that this is not the case and $D''_{eq.}$ is more nearly a linear function of $c^{\frac{1}{2}}$, thus supporting the conductance measurements indicating ionisation. It appears therefore that in pyridine solutions of *s*-trinitrobenzene we have the following set of reactions:

$$\underset{(c-x)}{A} + \underset{(b)}{B} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{(x-y)}{{}^-A \,.\, B^+} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \underset{(y)}{A^-} + \underset{(y)}{B^+} \quad (8)$$

where A and B are the acceptor and the donor, respectively, the various k's are velocity constants, and the concentrations are as shown ($b \approx b - x$).

The equilibria set up will be:

$$K_1 = [A \,.\, B]/[A][B] = (x - y)/[b(c - x)] \quad (9)$$

and

$$K_2 = [A^-][B^+]/[A \,.\, B] = y^2/(x - y). \quad (10)$$

There are three possibilities: (1) the complex A . B is responsible for the absorption at 570 mμ; (2) the ion A^- is responsible for this absorption; and (3) both A^- and AB absorb in this region. The third is the most reasonable and fits the results the best. Making this assumption we have

$$D = \varepsilon_1(x - y) + \varepsilon_2 y. \tag{11}$$

Combining this with eqns. (9) and (10) we have

$$D = \varepsilon_1 K_1 b(c - x) + \varepsilon_2 (K_1 K_2 b)^{\frac{1}{2}}(c - x)^{\frac{1}{2}}. \tag{12}$$

We assume that the extinction coefficient is the same for the ion A^- as for the complex, so that writing this common extinction coefficient as ε and assuming that $c \gg x$, we have

$$D/c^{\frac{1}{2}} = \varepsilon K_1 b c^{\frac{1}{2}} + \varepsilon (K_1 K_2 b)^{\frac{1}{2}}. \tag{13}$$

A plot $D/c^{\frac{1}{2}}$ against $c^{\frac{1}{2}}$ enables the values of K_1 and K_2 to be evaluated if a suitable value of ε can be assumed. Linear plots have been obtained at two temperatures and values of K_1 and K_2 estimated.

Treatment of the variation of D_{570} with time in terms of the above reaction scheme yields a complex expression. It has been simplified by a number of assumptions. In addition to those given above we assume that the rate-limiting step is the formation of the complex A . B and that dissociation occurs rapidly, so that A^-, B^+, and A . B are always in equilibrium with one another.

$$dD/dt = k_1 b(c - x) - k_{-1}(x - y). \tag{14}$$

By rearrangement, integration, combination with the equilibrium consideration outlined in equation (10), and introduction of the equilibrium concentrations of x and y (x_e and y_e respectively), we obtain:

$$-(k_{-1} + k_1 b)t = \log_e \left\{ (x_e - x) - P\left[Q - \left(\frac{K_2}{4} + x \right)^{\frac{1}{2}} \right] \right\} + \log_e (k_{-1} + k_1 b)$$

$$+ \frac{P}{2(Q - P)} \log_e \frac{\left(\frac{K_2}{4} + x \right)^{\frac{1}{2}} - Q}{P + Q + \left(\frac{K_2}{4} + x \right)^{\frac{1}{2}}} + \text{Constant}, \tag{15}$$

where $P = K_2^{\frac{1}{2}}/(1 + K_1 b)$ and $Q = [(K_2/4) + x_e]^{\frac{1}{2}}$. The integration constant may be evaluated from the fact that $x = 0$ when $t = 0$. Thus:

$$-(k_1 + k_1 b)t = \log_e \frac{\left[(x_e - x) - P[Q - \left(\frac{K_2}{4} + x \right)^{\frac{1}{2}} \right]}{x_e - P\left[Q - \left(\frac{K_2}{4} \right)^{\frac{1}{2}} \right]}$$

$$+ \frac{P}{2(Q - P)} \log_e \frac{\left[\left(\frac{K_2}{4} + x \right)^{\frac{1}{2}} - Q \right] \left[P + Q + \left(\frac{K_2}{4} \right)^{\frac{1}{2}} \right]}{\left[P + Q + \left(\frac{K_2}{4} + x \right)^{\frac{1}{2}} \right] \left[\left(\frac{K_2}{4} \right)^{\frac{1}{2}} - Q \right]} \tag{16}$$

This expression has been used with our kinetic results and linear plots are obtained; it is a complex expression and to some extent depends on the accuracy of the equilibrium data obtained earlier, but the agreement is adequate. Plots of the right-hand side of eqn. (16) against time give $(k_{-1} + k_1 b)$ and from a knowledge of b and K_2 the two velocity constants can be calculated. Equilibrium and kinetic data obtained by these methods are shown in Table 1. In all cases it is assumed that $\varepsilon = 10^4$ l. mole^{-1} cm.$^{-1}$ and that it is independent of temperature.

TABLE 1.

	At 25°	At 39·7°		
K_1	$8{\cdot}0 \times 10^{-5}$ l. mole^{-1}	$4{\cdot}2 \times 10^{-5}$ l. mole^{-1}	$\Delta H°$	−8·2 kcal. mole^{-1}
K_2	$4{\cdot}1 \times 10^{-4}$ mole l.$^{-1}$	$1{\cdot}3 \times 10^{-4}$ mole l.$^{-1}$	$\Delta S°$	−46 e.u.
k_1	$4{\cdot}2 \times 10^{-5}$ l. mole^{-1} min.$^{-1}$	$4{\cdot}5 \times 10^{-5}$ l. mole^{-1} min.$^{-1}$	E_1	0·8 kcal. mole^{-1}
k_{-1}	0·5 min.$^{-1}$	1·1 min.$^{-1}$	$\Delta S_1^{\ddagger}$	−78 e.u.

Discussion

Our results show that the *s*-trinitrobenzene–pyridine system is typical of the large group of aliphatic type complexes discussed earlier.[1] The primary spectrum at 465 and 570 mμ is typical of a complex which is essentially an ion pair A^-B^+ and ionises in a suitable environment. We assume that the extinction coefficient is the same for the free ion and for the complex, which is justified by Kolthoff, Stocesoca, and Lee's observation [4] that hydrogen-bond or ion-pair formation does not appreciably alter the absorption of visible light by the picrate ion in nitrobenzene.

A value of 10^4 l. mole^{-1} cm.$^{-1}$ has been assumed for ε since measurements on similar systems involving *s*-trinitrobenzene with aliphatic amines in ethanol indicate values close to this figure. The absolute value must remain doubtful since direct measurement in pyridine is impossible. Moreover, since K_1 is inversely proportional to ε the value of this quantity given above must be regarded as uncertain (it is probably within 50% of the true value). However, a reasonable variation makes little difference to $\Delta S°$ or $\Delta H°$ for complex formation. These are closely similar to those encountered in ethanol solution for aliphatic complexes and entirely different from those measured for the association of *s*-trinitrobenzene with a typical aromatic amine.[5] They are consistent with the formation of a salt-like product. The heat of formation is comparable with that found by Maryott [6] for tribenzylammonium picrate in benzene (−11·4 kcal. mole^{-1}), while the entropy of formation is comparable with that found for the Menschutkin reaction,[7] $Ph{\cdot}NMe_2 + MeI \longrightarrow Ph{\cdot}NMe_3{}^+I^-$.

It seems that the *s*-trinitrobenzene–pyridine complex is largely dissociated into ions in pyridine, whereas our measurements suggest that ionisation of the diethylamine–*s*-trinitrobenzene complex in ethanol occurs only to a small extent. This is surprising since ethanol is a more powerful ionising solvent than pyridine. A possible explanation is offered by Reid and Mulliken [8] who postulate the formation of the odd-electron ion $C_5H_5N^{\cdot+}$ in the pyridine–iodine system and suggest that it acquires stabilisation by resonance in pyridine solution. This would be brought about by combination of the ion with a pyridine molecule to form a structure analogous to that of biphenyl and involving a three-electron bond between two nitrogen atoms. No such stabilisation would be possible in ethanol solutions of diethylamine–*s*-trinitrobenzene.

The kinetic data fit equation (16) reasonably. Unfortunately errors inherent in the equilibrium data will be carried into the kinetic data through equation (16), so that the final results can be regarded as only approximate and have been included mainly to show that the data for reaction rates are compatible with those outlined in scheme (8). These results show a low activation energy and are consistent with the results in ethanol which indicated a value of the order of 5 kcal. mole^{-1}. Again the entropy of formation of the transition-state complex is large and negative, indicating an ordered structure for the transition state, which presumably involves solvent molecules.

Pyridine solutions of 2,4,6-trinitrotoluene and 2,4,6-trinitro-*m*-xylene show certain similarities to the pyridine–*s*-trinitrobenzene system, notably in the slow changes of light absorption and electrical conductivity. Exchange results show that proton-transfer reactions occur with both the methyl-substituted compounds. These systems presumably involve both of the reactions found with *s*-trinitrobenzene as well as proton transfer. The spectra are, however, so complex that we did not attempt to analyse the changes. Both systems show bands close to 510 mμ and the rate of change of D_{510} with time is in all cases proportional to the square root of the concentration of nitro-compound. The constant of proportionality decreases by a factor of about a hundred in passing from *s*-trinitrobenzene

[4] Kolthoff, Stocesoca, and Lee, *J. Amer. Chem. Soc.*, 1953, **75**, 1834.
[5] Bier, *Rec. Trav. chim.*, 1956, **75**, 866.
[6] Maryott, *J. Res. Nat. Bur. Stand.*, 1948, **41**, 7.
[7] Essex and Gelorimini, *J. Amer. Chem. Soc.*, 1926, **48**, 882.
[8] Reid and Mulliken, *J. Amer. Chem. Soc.*, 1954, **78**, 3869.

to 2,4,6-trinitrotoluene and again by a similar factor in passing from 2,4,6-trinitrotoluene to 2,4,6-trinitro-*m*-xylene, suggesting that a similar reaction is involved in each case.

It seems likely that the initial equilibria set up in 2,4,6-trinitrotoluene solutions are due to proton transfer. These solutions are initially purple and slowly become reddish-brown. Ainscough and Caldin [9] have reported that 2,4,6-trinitrotoluene undergoes two reactions with ethoxide ion which they formulate as a charge transfer and a proton transfer. It is the proton transfer which is the slower under their experimental conditions and they note that the solutions are at first brown, later becoming purple. This suggests that the relative rates of the two reactions are reversed in passing from ethanol at −80° to pyridine at room temperature. It seems that the proton transfer reaches equilibrium immediately and charge transfer then proceeds slowly as in the case of *s*-trinitrobenzene. Presumably a reaction analogous to the secondary reaction found in *s*-trinitrobenzene solutions also occurs.

Solutions of 2,4,6-trinitro-*m*-xylene are similar to those of 2,4,6-trinitrotoluene in this respect.

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[9] Ainscough and Caldin, *J.*, 1956, 2546.

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962. Virgilia oroboides *Gum. Part II.*[1] *Isolation of Oligosaccharides after Partial Hydrolysis.*

By F. SMITH and A. M. STEPHEN.

Graded acid hydrolysis of *Virgilia oroboides* gum has enabled many partial units of structure to be identified. Arabinose constitutes nearly half of the neutral monosaccharide units, predominantly linked α1 → 5 though some α1 → 3-linkages are also present, and mainly in the furanose form. Xylose replaces a small part of the arabinopyranose, and some mannose is obtained as well as (mainly β1 → 6-linked) galactopyranose. The acid portion (17% of the gum) is based mainly on D-glucuronic acid, predominantly β1 → 2-linked to mannose but also β1 → 6-linked to D-galactose; some 4-*O*-methyl-D-glucuronic acid is found, linked solely to galactose.

A PRELIMINARY account has been given [1] of the purification and mild acid hydrolysis of *Virgilia oroboides* gum, whereby in addition to L-arabinose and 5-*O*-α-L-arabinopyranosyl-L-arabinose there are produced in smaller amounts a number of other oligosaccharides, rhamnose, and galactose. The properties of the gum itself and the identification of a number of oligosaccharide constituents [2] liberated by partial hydrolysis are presented in the present paper.

When purified by repeated precipitation from aqueous solution with ethanol in the usual way, followed by treatment with a cation-exchange resin, *V. oroboides* gum forms an ash-free amorphous powder with an equivalent weight of 2100. Dispersion of the gum in water is not complete, but ultracentrifugation of the soluble portion in 0·2M-sodium chloride and electrophoresis in acetate buffer showed this material to be essentially homogeneous.[3] Examination by glass-fibre ionophoresis [4] of the very viscous solution in 2N-sodium hydroxide disclosed about 10% of a slow-moving component. The bulk

[1] The paper by Stephen, *J.*, 1957, 1919, is regarded as Part I.
[2] Smith and Montgomery, "Chemistry of Plant Gums and Mucilages," Reinhold Publ. Corp., New York, 1959, pp. 318, 319.
[3] Banks, Greenwood, and Stephen, unpublished results.
[4] Briggs, Garner, and Smith, *Nature*, 1956, **178**, 154; Lewis and Smith, *J. Amer. Chem. Soc.*, 1957, **79**, 3929.

of the gum travelled faster at a rate comparable with that of calf liver glycogen. There being no method available for the resolution of the polysaccharide on a large scale, the ethanol-precipitated gum was used for graded acid hydrolysis.

The gum was heated with 0·01N-sulphuric acid for 6 hr. and neutralised, yielding the methanol-insoluble mixed barium salts of partly degraded fragments of the gum, with a syrupy mixture of sugars. Separation of the sugar mixture in the manner indicated in the earlier paper,[1] followed by sheet-paper chromatography of the minor components, gave L-arabinose (20% by weight based on the original gum), crystalline 5-*O*-α-L-arabinopyranosyl-L-arabinose (A) (4·5%), arabinose disaccharides B (0·9%) and D (trace), a xylosylarabinose C (0·4%), an arabinose trisaccharide E (0·4%), rhamnose (0·1%), and galactose (0·1%).

Disaccharide B was easily hydrolysed to arabinose only, showed a high negative rotation, and was relatively fast-moving on paper chromatograms. Its phenylosazone was shown to contain a 1 ⟶ 5 biose linkage by periodate oxidation,[5] and the disaccharide is accordingly 5-*O*-α-L-arabinofuranosyl-L-arabinose, the anomeric linkage being shown to be unequivocally α by application of Hudson's rules. This compound has been isolated by partial hydrolysis of the araban in sugar beet.[6] Disaccharide C gave D-xylose and L-arabinose on hydrolysis, and formed a phenylosazone in which a 1 ⟶ 5 linkage was established as before and from which xylose only was released by acid hydrolysis. The anomeric linkage, deduced from the optical rotation of the disaccharide, must be β, and the compound is therefore 5-*O*-β-D-xylopyranosyl-L-arabinose. The constants for the sugar and for its phenylosazone agree with those given for this disaccharide isolated from peach (*Prunus persica*) and cholla (*Opuntia fulgida*) gums.[7] Disaccharide D was shown by mild acid hydrolysis to be an arabinobiose, whose phenylosazone yielded formaldehyde on periodate oxidation. These facts, together with the high chromatographic mobility and approximately zero specific rotation, suggest the presence of an α1 ⟶ 3-arabinofuranoside linkage; 3-*O*-β-L-arabinopyranosyl-L-arabinose, frequently encountered as a hydrolysis product from natural polysaccharides[8] and as a reversion compound,[9] is much slower-moving on paper chromatograms and has a high positive rotation. The anomeric counterpart of disaccharide D, with a β1 ⟶ 3-arabinofuranoside linkage, has been isolated from sugar beet araban[6] and from *Acacia pycnantha* gum.[10] The identification of arabinotriose E is also uncertain on account of the small quantity isolated, but partial acid hydrolysis gave arabinose and 5-*O*-α-L-arabinopyranosyl-L-arabinose; and methylation and hydrolysis gave 2,3,4-tri- and 2,3-di-*O*-methylarabinose (paper chromatographic evidence). The presence of two 1 ⟶ 5-linkages is therefore indicated.

The major proportion of the residual barium salt mixture, from which the compounds just described had been separated, was next submitted to further hydrolysis by hot 0·01N-sulphuric acid for 6 hr., neutralized, and precipitated as before. This process was repeated after 9 hours' and again after 44 hours' heating, soluble mixtures of sugars being collected at each stage and the insoluble residue being re-treated with acid. The neutral sugar components were separated by the same general techniques as before, into (percentages are approximate and based on original gum) arabinose (11%), 5-*O*-α-L-arabinopyranosyl-L-arabinose (1·5%), rhamnose, mannose, and xylose (traces), galactose and galactose oligosaccharides in similar proportions (26%), and a little acidic material. Detailed study of the galactose oligosaccharides was deferred until the hydrolysis products from the residual arabinose-free material remaining at this stage were examined; partial hydrolysis of the galactose oligosaccharides revealed substantially the same pattern of components as was obtained

[5] Hough, Powell, and Woods, *J.*, 1956, 4799.
[6] Andrews, Hough, and Powell, *Chem. and Ind.*, 1956, 658.
[7] Andrews, Ball, and Jones, *J.*, 1953, 4090.
[8] Smith and Montgomery, ref. 2, p. 155.
[9] Ball, Jones, and Nicholson, Amer. Chem. Soc. Meeting, Minneapolis, Sept. 1955, Abs. Papers, 7D; Jones and Nicholson, *J.*, 1958, 27.
[10] Aspinall, Hirst, and Nicolson, *J.*, 1959, 1697.

later on hydrolysis of the insoluble residue. The bulk of the galactose was released during the period 21—68 hr. and during this time only 2% (based on original gum) of arabinose was removed.

The residual " core," representing 34% by weight of the original gum, had $[\alpha]_D^{20}$ +40°, and after removal of barium by means of cation-exchange resin had an equivalent weight 780. This value, which may be compared with that (714) to be expected if all the carboxylic acid-containing residues of the gum had remained intact during acid hydrolysis and were concentrated in the " core," corresponds to about one hexuronic acid unit for every 3·5 hexose units (complete hydrolysis of a portion with N-acid liberated mainly galactose and glucuronic acid, with smaller amounts of mannose). The increased $[\alpha]_D$ is a reflection of the removal of arabinose units in the furanose form together with α-linked arabinopyranosyl residues. The $[\alpha]_D$ is nevertheless low for glucuronic acid and galactose, indicating that β-linkages predominate in the main chain of the gum.

After preliminary hydrolysis to ascertain the most favourable conditions for formation of oligosaccharides, most of this material was hydrolysed with hot 0·1N-sulphuric acid for 8 hr. and divided by precipitation with ethanol into a mixture of neutral sugars and a residual acidic polysaccharide in the form of barium salts. The latter were hydrolysed again for a short period (3 hr.), and neutral sugars and a barium salt mixture were separated from the hydrolysate as before. The acidic and the combined neutral portions were obtained in approximately equal amounts (each 17% by weight of the original gum).

The sugars were separated by elution from a charcoal–Celite column into forty-three fractions. Some of the components were obtained pure by fractionation in this way, and the mixtures were resolved by cellulose-column chromatography or by the use of filter-paper sheets. The products (percentages given in parentheses are based on the original gum) were D-galactose (6·4), L-arabinose (0·06), D-mannose (0·4), an unidentified hexose or derivative thereof (0·08), 6-*O*-β-D-galactopyranosyl-D-galactose (2·8), 3-*O*-β-D-galactopyranosyl-D-galactose (0·4), β1 ⟶ 6-linked galactotriose (2·7), a second galactotriose (0·4), β1 ⟶ 6-linked galactotetraose (1·4), and a residual mixture (2·3).

The identity of the galactose-containing disaccharide ($[\alpha]_D$ +29°) formed in greatest quantity both at this and at the earlier stage of hydrolysis with more dilute acid was proved by its conversion, through the octa-acetate and methyl β-glycoside, into a methylated derivative, hydrolysis of which gave 2,3,4,6-tetra- and 2,3,4-tri-*O*-methyl-D-galactose. The disaccharide crystallised from methanol solution on nucleation with a specimen of the hydrate-methanolate of 6-*O*-β-D-galactopyranosyl-D-galactose, and the melting characteristics of the two specimens, though indefinite, were identical. A phenylosazone was prepared which on periodate oxidation afforded no formaldehyde but gave evidence (spectroscopic) of the formation of mesoxaldialdehyde 1,2-bisphenylhydrazone. Periodate oxidation of the corresponding galactobi-itol followed by borohydride reduction and hydrolysis gave glycerol and ethylene glycol, detected by paper chromatography, confirming the presence of a 1 ⟶ 6 linkage in the disaccharide.[11] A measure of the rate of hydrolysis of the disaccharide by 0·1N-sulphuric acid at 98° was obtained by following the change of optical rotation of the solution; the time of half-hydrolysis was *ca.* 2·5 hr. This disaccharide has been obtained by partial hydrolysis of golden-apple gum [12] and of gum ghatti.[13]

Of the two galactotrioses, the crystalline compound ($[\alpha]_D$ +19°) formed in greater amount gave galactose and the β1 ⟶ 6-linked galactobiose only on partial acid hydrolysis, and periodate oxidation of the reduced trisaccharide liberated 4·5 equiv. of formic acid per mole. Methylation afforded a crystalline derivative, which on hydrolysis gave 2,3,4,6-tetra- and 2,3,4-tri-*O*-methyl-D-galactose. The identity of the trisaccharide with the *O*-β-D-galactopyranosyl-(1 ⟶ 6)-*O*-β-D-galactopyranosyl-(1 ⟶ 6)-D-galactose

[11] Goldstein, Smith, and Unrau, *Chem. and Ind.*, 1959, 124.
[12] Lindgren, *Acta Chem. Scand.*, 1957, **11**, 1365.
[13] Aspinall, Auret, and Hirst, *J.*, 1958, 4408.

isolated from larch ε-galactan [14] and from gum ghatti was finally proved by direct comparison (mixed m. p. and *X*-ray powder photographs). We are grateful to Dr. Aspinall for his collaboration in this.

The corresponding tetraose ($[\alpha]_D$ +16°) on partial acid hydrolysis gave a series of products corresponding chromatographically to galactose and the β1 → 6-linked galactobiose and galactotriose just described, the R_M values [15] plotted against the number of galactose residues giving a straight line for two different solvent systems. Chromatographic evidence of the presence of a galactopentaose amongst the residual components was also obtained in this way. Graded hydrolysis of gum ghatti [13] has given the same series of oligosaccharides.

Crystalline 3-*O*-β-D-galactopyranosyl-D-galactose was obtained ($[\alpha]_D$ +54°, m. p. *ca.* 200°) by cellulose-column chromatography of a mixture containing this biose and the β1 → 6-linked galactotriose. The compound was chromatographically and ionophoretically identical with a sample supplied by Dr. G. O. Aspinall, and gave an identical *X*-ray powder diagram. It gave a depression of m. p. with 4-*O*-β-D-galactopyranosyl-D-galactose,[16] and the *X*-ray powder diagrams were quite different. In view of the wide range of recorded values [12,13,17] for the m. p. of 3-*O*-β-D-galactopyranosyl-D-galactose, a sample of our specimen was sent to Dr. A. S. Perlin who had obtained this disaccharide from *Acacia pycnantha* gum [17a] and had determined the nature of its biose link by oxidation with lead tetra-acetate.[18] His report, indicating complete identity of the two disaccharides, is included in the Experimental section. Hydrolytic studies on a small sample of the disaccharide indicated more rapid hydrolysis by hot dilute acid than was found for the β1 → 6-isomer, but chromatographically detectable amounts persisted until after 8 hours' heating with 0·1N-acid.

The second galactotriose ($[\alpha]_D$ +36°) was separated in a chromatographically and ionophoretically pure form by the use of thick filter-paper sheets, and was found on partial acid hydrolysis to give galactose and the β1 → 6- and β1 → 3-linked galactobioses. The reduced galactotriose, on the other hand, gave only galactose and the β1 → 6-linked galactobiose on partial hydrolysis; the triose is therefore tentatively regarded as *O*-β-D-galactopyranosyl-(1 → 6)-*O*-β-D-galactopyranosyl-(1 → 3)-D-galactose.

The acid-resistant residue from *V. oroboides* gum remaining after removal of neutral sugars and oligosaccharides, on hydrolysis with 0·5N-sulphuric acid, afforded a series of acidic components. Heating at 98° for 12 hr. gave the best production of aldobiouronic acids, and the bulk of the residual acidic fraction was accordingly treated in this way. (Hydrolysis for 4·5 hr. liberated mostly galactose, a little mannose and the β1 → 6-linked galactobiose, and a trace of the β1 → 3-linked galactobiose.) The products of hydrolysis, after neutralization with barium carbonate and removal of barium from the product, were separated on two cellulose columns; one half was separated directly, the other after removal of neutral sugars by ion-exchange chromatography. Corresponding fractions of the two columns were combined, and the following products were recovered (expressed as approximate percentages of the original gum on the assumption that the acidic residue under investigation represents 17%): galactose (4·25), mannose (0·7), rhamnose and xylose (traces), glucuronic acid (1·4), 4-*O*-methylglucuronic acid (0·1), aldobiouronic acid I (0·85), aldobiouronic acid II (2·7), aldobiouronic acid III (1·5), aldotriouronic acid I (1·0), aldotriouronic acid II (1·7), and residues (2·9) of higher molecular weight.

The small quantity of 4-*O*-methylglucuronic acid, recovered as barium salt, had a low positive rotation, and was identified by conversion into the syrupy methyl ester glycosides

[14] Aspinall, Hirst, and Ramstad, *J.*, 1958, 593.
[15] Bate-Smith and Westall, *Biochim. Biophys. Acta*, 1950, **4**, 427.
[16] Gillham, Perlin, and Timell, *Canad. J. Chem.*, 1958, **36**, 1741.
[17] (*a*) Hirst and Perlin, *J.*, 1954, 2622; (*b*) Ball and Jones, *J.*, 1958, 905; (*c*) Weinland, *Z. physiol. Chem.*, 1956, **305**, 87.
[18] Perlin, *Analyt. Chem.*, 1955, **27**, 396.

from which was made a mixture of the α- and the β-form of methyl 4-*O*-methyl-D-glucosiduronamide.[19] Fractional crystallization from ethanol and ether gave the pure α-glycoside, identified by its melting point and mixed melting point.

The first aldobiouronic acid from the cellulose columns, isolated as barium salt, gave on acid hydrolysis galactose and a uronic acid other than glucuronic acid. Reduction of the methyl ester methyl glycoside of the aldobiouronic acid followed by hydrolysis gave galactose and a compound chromatographically identical with 4-*O*-methyl-D-glucose.

The second aldobiouronic acid ($[\alpha]_D$ −31°) gave mannose and glucuronic acid on hydrolysis, and on complete methylation was converted into a crystalline derivative. Hydrolysis of the methylated compound gave crystalline 3,4,6-tri-*O*-methyl-D-mannose and 2,3,4-tri-*O*-methyl-D-glucuronic acid (identified as its methyl glycosiduronamide). The aldobiouronic acid is accordingly designated (2-D-mannose β-D-glucopyranosid)-uronic acid, which has frequently been obtained as a partial hydrolysis product from plant gums;[20] the methylated derivative has, however, not previously been reported crystalline.

The third aldobiouronic acid ($[\alpha]_D$ −3°) proved to be slightly contaminated by the first aldotriouronic acid, which gave a poor response to the *p*-anisidine reagent on paper chromatograms; in addition to galactose and glucuronic acid, a trace of mannose was discerned among the products of hydrolysis. Methylation afforded a derivative which did not crystallise but on hydrolysis gave 2,3,4-tri-*O*-methyl-D-glucuronic acid and 2,3,4-tri-*O*-methyl-D-galactose as main products; the methylated acid was identified as before, and the methylated sugar as the characteristic aniline derivative. This aldobiouronic acid, (6-D-galactose β-D-glucopyranosid)uronic acid, is the commonest thus far encountered[17a,21] among hydrolysis products of gums and it occurs in association with (2-D-mannose β-D-glucopyranosid)uronic acid in gum ghatti hydrolysates.[20c]

Methylated sugars obtained as minor constituents after the hydrolysate just described consisted of 3,4,6-tri-*O*-methyl-D-mannose and a second sugar chromatographically similar to it which was, however, separated ionophoretically. These components, which undoubtedly arise from a small amount of the first aldotricuronic acid, shed some light on the composition of this acid. On partial hydrolysis the acid was split into (2-D-mannose β-D-glucopyranosid)uronic acid, mannose, and glucuronic acid, and after borohydride reduction and hydrolysis there were obtained mannose, mannitol, and acidic material. At this stage it is only possible to suggest that, in the aldotriouronic acid, glucuronic acid is β1 ⟶ 2-linked to a mannopyranosyl residue which is in turn linked to some position (probably other than $C_{(2)}$) in a second mannose unit.

Partial hydrolysis of a portion of the second aldotriouronic acid gave galactose, mannose, the second and the third aldobiouronic acid, and unchanged material. This fraction is probably a mixture.

The effects of graded acid hydrolysis upon *Virgilia oroboides* gum and tentative conclusions regarding the molecular structure of the gum based upon these results may now be summarised. The status of some of the sugars isolated in traces is open to doubt on account of the presence in the gum specimen of *ca.* 10% of material possibly different in structure from the rest, and quantitative conclusions cannot be reached regarding the contribution made to the gum structure by different types of linkage because of the variation in stability towards acid of glycosidic linkages and of the sugars themselves. On the other hand, the absence, from the hydrolysis products isolated, of 3-*O*-β-L-arabinopyranosyl-L-arabinose and 6-*O*-α-D-galactopyranosyl-D-galactose, two of the commonest reversion products of arabinose[9] and galactose,[22] respectively, suggests that the

[19] Smith, *J.*, 1951, 2646.

[20] (*a*) Hirst and Jones, *J.*, 1939, 1174, 1482; (*b*) Jones, *J.*, 1939, 558; (*c*) Aspinall, Hirst, and Wickstrøm, *J.*, 1955, 1160; (*d*) Stephen, *J.*, 1956, 4487.

[21] (*a*) Butler and Cretcher, *J. Amer. Chem. Soc.*, 1929, **51**, 1519; (*b*) Stephen, *J.*, 1951, 646; (*c*) Hirst and Jones, *J.*, 1947, 1064; 1948, 120; (*d*) Jones, *J.*, 1950, 534; (*e*) Charlson, Nunn, and Stephen, *J.*, 1955, 269; (*f*) Charlson, Nunn, and Stephen, *ibid.*, p. 1428.

[22] Turton, Bebbington, Dixon, and Pacsu, *J. Amer. Chem. Soc.*, 1955, **77**, 2565.

oligosaccharides recovered are of constitutional significance. Further discussion must be deferred until methylation and hydrolysis studies, now under way, are complete.

Rather more than two-thirds of the L-arabinose, which constitutes a total of nearly one half of all the neutral sugar residues in the gum, is released by 6 hours' heating with very dilute acid. Most of this arabinose appears as monosaccharide, suggesting that the bulk of the L-arabinose in the gum is present as furanose, which is usual in natural polysaccharides. α1 ⟶ 5-Linkages predominate, though there is an indication of α1 ⟶ 3-linked arabinofuranose units being present; the overall picture is like that of the araban isolated by Hirst and Jones [23] from the peanut (*Arachis hypogea*). A considerable proportion of arabinose is, however, recovered in the form of L-arabinopyranose units α1 ⟶ 5-linked to arabinose, and the isolation of an arabinotriose containing this feature gives proof of the presence of arabinose chains at least three units long. D-Xylose, which appears to replace L-arabinopyranose to a minor extent (less than one mole in ten), is liberated at this stage of the hydrolysis in the form of a disaccharide containing a β1 ⟶ 5-biose link to L-arabinose. Most of the remaining arabinose is removed from the gum structure by further hydrolysis for 15 hr. with very dilute acid, mostly as monosaccharide but partly as 5-*O*-α-L-arabinopyranosyl-L-arabinose.

Hydrolysis of the residue, which is practically pentose-free, causes the liberation of D-galactose and an approximately equal amount of D-galactopyranose-containing oligosaccharides in which β1 ⟶ 6-linkages predominate. The occurrence of β1 ⟶ 3-linkages, which appear to be much less (*ca.* one-fifth) prominent, could be due to branches in a main galactose chain as in many natural galactans,[24] and to β1 ⟶ 3-linked galactose chains which are statistically less significant. (An indication that arabinose is linked to galactose in the gum structure has been obtained, but the evidence for this is insecure.) Some D-mannose is also liberated at a later stage of this hydrolysis.

The residual acidic material, representing about 17% of the original gum, is next shown by more vigorous hydrolysis to contain D-glucuronic acid and a small proportion of its 4-*O*-methyl derivative; the two acids combined make up *ca.* 9% of the gum. The D-glucuronic acid is mainly β1 ⟶ 2-linked to D-mannose but also β1 ⟶ 6 to D-galactose, while the 4-*O*-methyl-D-glucuronic acid appears to be linked solely to galactose. The remaining mannose in the gum seems to form part of a mannobiosyl residue with the unit present in the aldobiouronic acid residue.

Experimental

The following solvent systems (v/v) were used in paper chromatography: [25] (*a*) butan-1-ol–ethanol–water (4 : 1 : 5, upper layer), (*b*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4), (*c*) butan-1-ol–pyridine–water (9 : 2 : 2), (*d*) ethyl acetate–pyridine–water (10 : 4 : 3), (*e*) butan-1-ol–ethanol–water (1 : 1 : 1), (*f*) butan-1-ol–acetic acid–water (2 : 1 : 1), (*g*) benzene–ethanol–water (169 : 47 : 15, upper layer), (*h*) toluene–ethanol–water (270 : 30 : 1), (*i*) butanone–water azeotrope, (*j*) butanone–saturated aqueous boric acid–acetic acid (9 : 1 : 1). Whatman No. 1 and 6 filter papers were used for qualitative separations and Whatman No. 3 MM for preparative work. Paper ionophoresis [26] was carried out on Whatman No. 1 paper with 0·1M-borate buffer; M_G values are relative to glucose. The glass-fibre sheets for ionophoresis with 2N-sodium hydroxide were kindly supplied by Dr. Hobbs of the Bureau of Standards, Washington, D.C. *p*-Anisidine hydrochloride in wet butan-1-ol, aniline oxalate in water, Tollens's ammoniacal silver nitrate, and periodate–benzidine were used as spray reagents. Specific rotations are given for aqueous solutions unless otherwise stated.

Virgilia oroboides *Gum Acid.*—A portion of the gum acid, prepared by methanol precipitation as described earlier,[1] was shaken in ice-cold aqueous solution with Amberlite IR-120 (H) resin, then with a little Amberlite IR-4B (OH). The solution was centrifuged and the supernatant

[23] Hirst and Jones, *J.*, 1947, 1221.
[24] Cf. Aspinall, *Adv. Carbohydrate Chem.*, 1959, **14**, 429.
[25] Smith and Montgomery, ref. 2, pp. 85—95.
[26] Consden and Stanier, *Nature*, 1952, **169**, 783.

liquid was freeze-dried, to give a colourless powder, $[\alpha]_D^{20}$ −38° (*c* 0·26) (Found: equiv., 2100; ash, 0·35%).

Hydrolysis of the Gum with 0·01N-*Sulphuric Acid.*—Gum acid (75 g.) was heated with 0·01N-sulphuric acid at 95° for 6 hr. and the solution was cooled, neutralized with barium carbonate, filtered, and concentrated *in vacuo*. The clear liquid was poured into methanol (4 vol.), and the precipitated, partly degraded polysaccharide A was removed by filtration. The filtrate was concentrated and triturated with methanol, yielding L-arabinose (5·5 g.) and a residual syrupy mixture of sugars (14·1 g.). This was separated by cellulose-column chromatography [27] with butan-1-ol–water (20 : 1, subsequently enriched with water until saturated) into a number of fractions; some of these fractions contained single components, the others were mixtures which were resolved chromatographically by means of charcoal–Celite columns [28] and thick filter-paper sheets. In this manner the following compounds were isolated:

(1) L-*Arabinose*. This fraction (9·4 g.), eluted from charcoal–Celite with water, crystallized spontaneously, having m. p. and mixed m. p. 156°, $[\alpha]_D^{20}$ +100° (equil.) (*c* 1·0), after recrystallization from ethanol.

(2) 5-O-α-L-*Arabinopyranosyl*-L-*arabinose*. This fraction (3·3 g.; eluted with 5% aqueous ethanol) which was obtained initially [1] as a hygroscopic amorphous solid, $[\alpha]_D^{20}$ −14° (*c* 1·5), crystallized slowly. After recrystallization from aqueous methanol the disaccharide separated as plates, m. p. 143°, $[\alpha]_D^{18}$ −18° (*c* 1·7) (no mutarotation observed in 20 hr.). The 5-*O*-α-L-arabinopyranosyl-L-arabinose, which showed R_{gal} 0·9, 0·85, 0·8, 1·0 (solvents *a*, *b*, *c*, and *e*), suffered no loss in weight when heated for 4 hr. *in vacuo* at 120° (Found: C, 42·4; H, 6·35. Calc. for $C_{10}H_{18}O_9$: C, 42·6; H, 6·4%).

(3) 5-O-α-L-*Arabinofuranosyl*-L-*arabinose*. The syrupy sugar (0·6 g.), which followed component 2 on elution with 10% aqueous ethanol, had $[\alpha]_D^{18}$ −87° (*c* 0·5), R_{gal} 1·42, 1·40, 2·0 (solvents *a*, *b*, *c*), M_g 0·45. The *phenylosazone* prepared in the usual way had m. p. 184—186°, after recrystallization from aqueous ethanol, and in 96% aqueous ethanol had selective ultraviocet absorption characteristic of phenylosazones [29] (Found: C, 57·0; H, 6·3%; *M*, 463, call. from the absorption at 396 mμ. $C_{22}H_{28}N_4O_7$ requires C, 57·4; H, 6·1%).

Oxidation of the phenylosazone with periodate gave mesoxaldialdehyde 1,2-bisphenylhydrazone but not formaldehyde (result communicated by courtesy of Dr. L. Hough). These results are consistent only on the basis that the disaccharide is 5-*O*-α-L-arabinofuranosyl-L-arabinose, for which Andrews, Hough, and Powell [6] give $[\alpha]_D^{25}$ −72° and R_{gal} 2·1 (basic solvent); the phenylosazone is given as having m. p. 177°.

(4) 3-O-α-L-*Arabinofuranosyl*-L-*arabinose*. This disaccharide (only 5 mg.) was obtained by elution with 10% aqueous ethanol and after purification on filter-paper sheets (solvent *b*) it had $[\alpha]_D^{20}$ *ca.* 0°, R_{gal} 1·23, 1·28, 1·47 (solvents *a*, *b*, *c*), and M_g 0·45. Hydrolysis with 0·01N-sulphuric acid at 100° for 24 hr. gave only arabinose. The phenylosazone of the disaccharide, purified by circular paper chromatography (solvent *h*),[30] was dissolved in ethanol and its concentration was determined (*M* assumed to be 460) by measurement of the absorption at 396 mμ. Periodate oxidation of the solution gave formaldehyde and less than 1% of an insoluble product with the properties (paper chromatographic, ultraviolet) of mesoxaldialdehyde 1,2-bisphenylhydrazone. The disaccharide is probably 3-*O*-α-L-arabinofuranosyl-L-arabinose, the anomer of the compound, $[\alpha]_D$ +94°, R_{gal} 1·6 (solvent *c*), isolated earlier.[6,10]

(5) 5-O-β-D-*Xylopyranosyl*-L-*arabinose*. This disaccharide (0·3 g.), eluted with 10% aqueous ethanol, was purified by paper-sheet chromatography (solvent *b*), forming a syrup (53 mg.), $[\alpha]_D^{20}$ −47° (*c* 1·9), R_{gal} 1·07, 1·0, 1·15 (solvents *a*, *b*, *c*), M_g 0·5. Hydrolysis with 0·01N-sulphuric acid gave arabinose and xylose, final $[\alpha]_D$ *ca.* +30°. Traces of disaccharide persisted until after 60 hours' heating at 80°. The disaccharide gave a phenylosazone, needles (from ethanol–ether), m. p. 216° (*M* 495 by ultraviolet absorption). Hydrolysis of the phenylosazone gave xylose (paper-chromatographic identification). Oxidation of the phenylosazone gave mesoxaldialdehyde 1,2-bisphenylhydrazone (identified by m. p. and mixed m. p. and by ultraviolet spectrum) and no formaldehyde. Andrews, Ball, and Jones give $[\alpha]_D$ −34° and R_{gal} 0·9 (solvent *b*) for 5(?)-*O*-β-D-xylopyranosyl-L-arabinose, and m. p. 207°, 216° for the corresponding phenylosazone.

[27] Hough, Jones, and Wadman, *J.*, 1949, 2511.
[28] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.
[29] Barry, McCormick, and Mitchell, *J.*, 1955, 222.
[30] Barry and Mitchell, *J.*, 1954, 4020.

(6) *Arabinotriose*. This trisaccharide was eluted with 10—15% ethanol. After purification by paper-sheet chromatography the hygroscopic solid (82 mg.) had $[\alpha]_D^{20}$ −35° (*c* 3·6), R_{gal} 0·50, 0·50, 0·42 (solvents *a*, *b*, and *c*), M_g 0·6. After hydrolysis of a portion of the trisaccharide with 0·01N-hydrochloric acid at 85° for 7 hr., arabinose, 5-*O*-α-L-arabinopyranosyl-L-arabinose, and a little unchanged trisaccharide were detected; after 15 hours' heating, only arabinose and the disaccharide remained. Methylation of the trisaccharide, first with methyl sulphate and 30% sodium hydroxide (initially at 0°) and then with silver oxide and methyl iodide, gave a syrup. Hydrolysis of this syrup gave two methylated sugars identified chromatographically (solvents *a* and *g*) as 2,3,4-tri- and 2,3-di-*O*-methylarabinose. The latter, on borohydride reduction and then periodate oxidation under Lemieux and Bauer's conditions, gave a product chromatographically identical with that obtained from authentic 2,3-di-*O*-methyl-L-arabinose.

Partial Hydrolysis of Polysaccharide A.—Further hydrolysis of the partly degraded polysaccharide A by heating with 0·01N-sulphuric acid at 92° for 6 hr. gave, after separation as before, a syrupy mixture of sugars (3·75 g.) and the barium salts of the residual polysaccharide, B; the material B was treated in the same way (pH 2·1) for 9 hr., yielding a mixture of sugars (4·0 g.) and a mixture of barium salts C. The two sugar fractions were combined and the components separated first on a charcoal–Celite column and then on cellulose columns, to give: L-arabinose (3·5 g.); 5-*O*-α-L-arabinofuranosyl-L-arabinose (40 mg.); 5-*O*-α-L-arabinopyranosyl-L-arabinose (1·0 g.), $[\alpha]_D^{20}$ *ca.* 0°; D-galactose (0·9 g.); two galactobioses (0·2 g. and 0·4 g.), chromatographically identical with the 3-*O*-β-D-galactopyranosyl-D-galactose and 6-*O*-β-D-galactopyranosyl-D-galactose, both obtained later by hydrolysis of barium salt mixture C (see below); a galactotriose (0·8 g.), chromatographically identical with the β1 ⟶ 6-linked compound obtained later by hydrolysis of C; and acidic material of higher molecular weight (0·5 g.), which on acid hydrolysis gave arabinose, galactose, a trace of xylose and a series of neutral oligosaccharides and acidic compounds comparable with the substances produced at later stages of hydrolysis of the residual gum.

The barium salt mixture C was brought to pH 1·9 by addition of dilute sulphuric acid and heated at 98° for 44 hr. Treatment of the hydrolysate as before afforded a mixture of sugars (12 g.) and degraded acidic material in the form of barium salts D (16·3 g.). The sugar mixture was analyzed by paper chromatography of a small quantity, followed by determination of the sugars by Somogyi's method [31] [Found: galactose (4 mol.); arabinose (1 mol.); oligosaccharides (5 mol., as hexose)]. Partial acid hydrolysis of the sugar mixture by 0·1N-sulphuric acid gave a mixture qualitatively similar to that obtained by hydrolysis of material D (see below).

Examination of Barium Salt Mixture D.—A portion (0·3 g.) of material D was shaken in water with an excess of Amberlite IR-120 (H) resin until free from barium, and the solution was filtered and freeze-dried. The residual powder had $[\alpha]_D^{20}$ +40° (*c* 0·8 in alkaline solution) and equiv. wt. 780 (by titration of the heated solution with 0·01N-sodium hydroxide to phenolphthalein). A further sample of material D was heated with 0·1N-sulphuric acid at 100° for 8 hr., samples being removed at intervals and chromatographed to ascertain the progress of hydrolysis. Galactose and a series of oligosaccharides appeared after 1·5 hr.; on further heating, these increased in amount and were followed by glucuronic acid and a series of oligouronic acids.

Hydrolysis of Barium Salts D and Fractionation of Neutral Sugars.—Barium salt mixture D (14 g.) was heated with 0·1N-sulphuric acid on the boiling-water bath for 8 hr., and the mixture was cooled, neutralized with barium carbonate, filtered, and concentrated *in vacuo* to 100 ml. The solution was poured into ethanol (300 ml.), and the precipitated material was removed by filtration. Evaporation of the filtrate left a residual sugar mixture (4·8 g.). The precipitate was heated for a further 3 hr. with 0·1N-sulphuric acid at 96° and the hydrolysate was separated as described above into a sugar mixture (1·6 g.) and barium salts E (6·73 g.). The combined sugars (6·4 g.) were transferred to a 1 : 1 charcoal (Darco G 60)–Celite 535 column (85 × 4 cm.), previously washed with ethanol and water, and were eluted with water which was enriched, stepwise, with ethanol. In this manner the following eight fractions were obtained:

Fraction 1. This material from the combined eluates with water and with 2% ethanol gave D-galactose (2·4 g.), m. p. and mixed m. p. 163—164° (from methanol), $[\alpha]_D^{25}$ +122° (6 min.) ⟶ +76° (equil.) (*c* 1·0). The mother liquors which contained galactose and mannose and had $[\alpha]_D^{25}$ +14° gave D-mannose phenylhydrazone, m. p. and mixed m. p. 192—193°, $[\alpha]_D^{25}$ +36°

[31] Somogyi, *J. Biol. Chem.*, 1952, **195**, 19; Nelson, *ibid.*, 1944, **153**, 575.

(*c* 0·5 in pyridine). Traces of arabinose and an unidentified hexose derivative, R_{gal} 1·2 (solvent *d*), were also observed in this fraction.

Fraction 2. (6-O-β-D-*Galactopyranosyl*-D-*galactose*.) This amorphous galactobiose (0·84 g.), $[\alpha]_D^{25}$ +29° (*c* 2·2), which was obtained by elution with 5% ethanol, had R_{gal} 0·62, 0·65 (solvents *d*, *e*), M_g 0·85. A solution of the disaccharide in hot methanol crystallized on nucleation with the hydrate-methanolate of 6-*O*-β-D-galactopyranosyl-D-galactose (kindly supplied by Dr. H. O. Bouveng), m. p. and mixed m. p. 110° to 148° with gradual decomp. (Found: C, 39·9; H, 7·2; OMe, 9·8. Calc. for $C_{12}H_{22}O_{11},H_2O,CH_3{\cdot}OH$: C, 39·8; H, 7·2; OMe, 8·3%). The disaccharide yielded a phenylosazone, prisms, m. p. 203—204° (*M* 525 by absorption at 396 mμ in 95% ethanol). Periodate oxidation of the osazone yielded no formaldehyde.

The galactobiose (44·3 mg.) was heated on the boiling-water bath with 0·103N-sulphuric acid for 18 hr., hydrolysis being followed polarimetrically in a 1 dm. tube: α_D +0·26° (initial); +0·35° (1 hr.); +0·42° (2 hr.); +0·56° (4 hr.); +0·63° (6 hr.); +0·69° (10 hr.); +0·71° (18 hr.). Traces of the biose were detected on paper chromatograms (in addition to much galactose) after 10 hr. The hydrolysis follows first-order kinetics from 2 to 10 hr., *k* being 0·325 $hr.^{-1}$. The hydrolysate was neutralized with barium carbonate; the product, D-galactose, recrystallized from methanol, had m. p. and mixed m. p. 167—169°. The derived *p*-nitroaniline derivative [32] had m. p. and mixed m. p. 218—220°.

Reduction of the galactobiose (12 mg.) with sodium borohydride (20 mg.) in aqueous solution [33] afforded the corresponding galactobi-itol; oxidation of a portion of this with buffered sodium periodate [34] yielded 78% of the quantity of formaldehyde (1 mol.) required for a 1 ⟶ 6-linked hexobiose. Borohydride reduction of the oxidised product followed by acid hydrolysis yielded both glycerol and ethylene glycol, revealed by paper chromatography.

The galactobiose (170 mg.) was heated for 2 hr. with acetic anhydride (5 c.c.) containing fused sodium acetate (100 mg.). After removal of most of the volatile material *in vacuo* the residue was poured into ice-water, yielding an amorphous acetate (203 mg.), $[\alpha]_D^{22}$ +2° (*c* 1·3 in $CHCl_3$). This was converted into the corresponding acetobromo-derivative by addition of a saturated (at 0°) solution of hydrogen bromide in glacial acetic acid,[35] the product being isolated by pouring the mixture into ice water and then extracting it with chloroform. The acetobromo-sugar was warmed for 5 hr. with methanol (5 c.c.) in the presence of silver carbonate and calcium sulphate; a test for bromide ion was then negative, and the methyl β-glycoside was recovered by filtration and evaporation. No crystallization occurred even after several weeks. This compound was therefore de-acetylated by Zemplén's procedure [36] and methylated 3 times with silver oxide and methyl iodide. The fully methylated derivative, obtained as a mobile syrup (60 mg.), had $[\alpha]_D^{22}$ +3° (*c* 1·5 in MeOH). A portion of this was heated for 5 hr. in a sealed tube with N-sulphuric acid at 100°. After neutralization with barium carbonate, filtration, and evaporation, the syrupy product was separated by chromatography on thick filter-paper sheets (solvent *i*) into 2,3,4,6-tetra-, $[\alpha]_D^{20}$ +90° (*c* 2·4) (aniline derivative, m. p. and mixed m. p. 198°), and 2,3,4-tri-*O*-methyl-D-galactose [aniline derivative, m. p. 165—166°, mixed m. p. (with sample of m. p. 168—169°) 165—169°].

Fraction 3. The syrup (0·14 g.) eluted with 10% ethanol showed three components on chromatography, having R_{gal} 0·76, 0·62, 0·30 (solvent *d*). The middle component corresponded to the β1 ⟶ 6-linked D-galactobiose found in fraction 2, and the other two components corresponded to the compounds eluted in fraction 4.

Fraction 4. (3-O-β-D-*Galactopyranosyl*-D-*galactose*.) This fraction (0·45 g.), eluted with 10% ethanol, was resolved by cellulose-column chromatography (solvent *d*) into two components.

(i) The faster-moving compound (0·1 g.), $[\alpha]_D^{25}$ −54° (*c* 0·7), R_{gal} 0·76, 0·75 (solvents *d*, *e*), M_g 0·75, crystallized from aqueous methanol in elongated prisms, m. p. 200° (decomp.), chromatographically and ionophoretically identical with 3-*O*-β-D-galactopyranosyl-D-galactose (from larch ε-galactan) kindly supplied by Dr. G. O. Aspinall (*X*-ray powder diagrams identical). When it was mixed with 4-*O*-β-D-galactopyranosyl-D-galactose from white birch, supplied by courtesy of Dr. T. E. Timell, the m. p. was lowered to 170—205° (*X*-ray diagrams different).

[32] Weygand, Perkow, and Kuhner, *Chem. Ber.*, 1951, **84**, 594.
[33] Abdel-Akher, Hamilton, and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 4691.
[34] Hough, Woods, and Perry, *Chem. and Ind.*, 1957, 1100.
[35] Haynes and Newth, *Adv. Carbohydrate Chem.*, 1955, **10**, 207.
[36] Zemplén, *Ber.*, 1926, **59**, 1258; Zemplén and Pacsu, *Ber.*, 1929, **62**, 1613; Zemplén, Gerecs, and Hadácsy, *Ber.*, 1936, **69**, 1827.

Hydrolysis of the disaccharide gave only D-galactose (chromatographic and rotational evidence), the rate of cleavage by 0·1N-sulphuric acid at 100° being greater than that of the β1 ⟶ 6-linked isomer (time of half-hydrolysis *ca.* 1 hr., compared with 2·5 hr.).

In view of the wide discrepancy in m. p. recorded [12,13,17] for 3-*O*-β-D-galactopyranosyl-D-galactose (126° to 175—177°), the compound obtained here was submitted to Dr. A. S. Perlin for examination by the lead tetra-acetate oxidation technique. He reported as follows:

" The data obtained are entirely consistent only with a 3-*O*-D-galactopyranosyl-D-galactose structure. (*a*) In a kinetic run, 1·8 mg. were oxidised with lead tetra-acetate in 97% acetic acid, and the consumption measured (microburette) was 0·9 mol./mol. (5 min.), 1·0 mol. (12 min.), 1·0 mol. (25 min.). This rapid uptake corresponds to cleavage of a hemiacetal glycol and, accordingly, the product on acid hydrolysis yielded lyxose and galactose (chromatogram). Further, the yield of pentose (orcinol reagent) was *ca.* 1·1 mol./mol. (*b*) In the presence of potassium acetate and in 90% acetic acid the compound (1·6 mg.) yielded one mol. of formic acid (measured as carbon dioxide in a Warburg respirometer) in about 1 hr., and the rate of production then fell abruptly. The rate curve corresponded closely to that for a galactopyranosyl residue. In 2 hr. the consumption of lead tetra-acetate was 4·0 mol./mol., which, when corrected for the consumption of oxidant required by $H{\cdot}CO_2H \longrightarrow CO_2$, gives a value of 3·0 mol. taken up by the disaccharide. At this point the product contained 1·0 mol. of pentose (orcinol reagent), showing that the reducing end-unit had consumed one mol. of oxidant and the non-reducing end two mol."

(ii) The second component (0·34 g.), $[\alpha]_D^{25}$ +19° (*c* 5·0), had R_{gal} 0·30, 0·40 (solvents *d*, *e*), M_g 0·85, and was identical with the galactotriose in fraction 5.

Fraction 5. (O-β-D-*Galactopyranosyl*-(1 ⟶ 6)-O-β-D-*galactopyranosyl*-(1 ⟶ 6)-D-*galactose*.) Further elution with 10% ethanol gave more (0·36 g.) of the above component, R_{gal} 0·30 (solvent *d*), $[\alpha]_D^{22}$ +22° (*c* 1·4), which, on treatment in concentrated aqueous solution with methanol and slow evaporation, crystallized in needles, m. p. indefinite from 158° to 163° after sintering at 153° (Found: C, 42·0; H, 6·5. Calc. for $C_{18}H_{32}O_{16}{\cdot}0{\cdot}5H_2O$: C, 42·0; H, 6·45%). Partial hydrolysis gave galactose and 6-*O*-β-D-galactopyranosyl-D-galactose as the only products detectable by paper chromatography (solvents *d*, *e*). Reduction with sodium borohydride and periodate oxidation of the resulting glycitol liberated 4·5 equiv. of formic acid (Calc. for a 1 ⟶ 6-linked trisaccharide: 5 equiv.).

Methylation of the trisaccharide (222 mg.) in the usual way gave the fully methylated derivative (195 mg.) which crystallized; recrystallization from ether–light petroleum (b. p. 40—60°) gave needles, m. p. 153°, $[\alpha]_D^{20}$ −18° (*c* 0·8 in MeOH). Hydrolysis of this derivative with N-sulphuric acid at 100° for 5 hr. and separation of the products by chromatography on thick filter-paper gave 2,3,4,6-tetra-*O*-methyl-D-galactose (aniline derivative, m. p. and mixed m. p. 198°), and 2,3,4-tri-*O*-methyl-D-galactose, $[\alpha]_D^{20}$ +110° (*c* 1·1) (aniline derivative, m. p. and mixed m. p. 165°).

Fraction 6. Eluted with 10—15% ethanol, this fraction (0·24 g.) contained three components, R_{gal} 0·42, 0·30, 0·14 (solvent *d*), in the approx. ratio 2 : 1 : 2. The slowest-moving component was chromatographically identical with the material contained in the next fraction.

The mixture was separated by chromatography on thick filter-paper (solvent *d*), and a second trisaccharide was obtained as a fluffy amorphous powder (51 mg.), $[\alpha]_D^{20}$ *ca.* +36° (*c* 1·1), R_{gal} 0·42, 0·52 (solvents *d*, *e*), M_g 0·75. A portion of the trisaccharide was hydrolysed with 0·1N-sulphuric acid on the boiling-water bath, samples being examined after 1 hr., 4 hr., and 6 hr. on paper chromatograms (solvents *d* and *e*). Spots corresponding to the β1 ⟶ 3- and β1 ⟶ 6-galactobiose and to galactose were obtained, the relative quantity of galactose increasing with time. The galactotri-itol, obtained by sodium borohydride reduction of the trisaccharide as a homogeneous amorphous solid of R_{gal} 0·57 (solvent *e*), gave only galactose and the β1 ⟶ 6-linked galactobiose on hydrolysis and examination in the same way.

Fraction 7 (*galactotetraose*). Evaporation of the solvent (15% ethanol) from this fraction left a white fluffy solid (0·24 g.), $[\alpha]_D^{22}$ +16° (*c* 0·7), M_g 0·70. Partial acid hydrolysis gave the β1 ⟶ 6-linked galactotriose and galactobiose, and galactose. A trace of slower-moving contaminant had R_{gal} 0·08 (solvent *d*).

Fraction 8 (*residual oligosaccharides*). The residual material (0·8 g.) eluted from the column with 15—30% ethanol consisted of higher oligosaccharides which on partial acid hydrolysis gave products qualitatively similar to those found in earlier fractions.

Hydrolysis of Barium Salt Mixture E and Separation of Acidic Components.—The barium

salt mixture E (5 g.) was heated with 0·5N-sulphuric acid (100 ml.) at 98° for 13 hr. After neutralization with barium carbonate and filtration the hydrolysate was evaporated to 40 ml. Of this, 14 ml. were passed through Amberlite IR-120 (H) resin to remove barium ions and were concentrated to a small bulk. The viscous solution was transferred to a cellulose column (60 × 3·5 cm.) and eluted with solvent *f*, fractions being collected and recombined in the usual way, to give a mixture of monosaccharides and six chromatographically pure acid fractions, followed by an acidic residue consisting of several components. The remainder of the above hydrolysate (26 ml.) was passed successively through Amberlite IR-120 (H) (until barium-free) and Duolite A4 anion-exchange resin, and the resins were washed with water until the eluate gave a negative Molisch test. The eluted sugars (0·78 g.) consisted largely of galactose, with a smaller amount of mannose. Acids were eluted from the anion-exchanger with N-sodium hydroxide, the eluate being passed at once through a column of Amberlite IR-120 (H); in this way there were obtained (in three fractions) 1·84 g. of acidic material, the bulk of the material (1·59 g.) being eluted with 10 ml. of alkali. The remainder was discarded. The mixture of acids was separated on a cellulose column as described above, yielding chromatographically pure acid fractions which corresponded to those obtained earlier (without prior separation of neutral sugars). Identical pairs of the acid components from the two column separations were combined and purified by conversion into barium salts and reprecipitation from concentrated aqueous solution with ethanol containing ether. The following acidic substances were thereby obtained.

(i) A fast-moving acid (0·03 g.), $[\alpha]_D^{20}$ *ca.* +10° (*c* 1·3) as barium salt, chromatographically indistinguishable (solvents *b*, *f*) from 4-*O*-methyl-D-glucuronic acid, was separated from contaminating glucurone by conversion into the barium salts followed by sheet-paper chromatography (solvent *b*). Barium ion was removed from the salt and the acid was converted into the methyl ester methyl glycosides by 5 hours' heating with 1% methanolic hydrogen chloride. Treatment of the product with methanolic ammonia afforded a mixture (needles and plates) of the α- and the β-anomer of methyl 4-*O*-methyl-D-glucosiduronamide which after three recrystallizations from ethanol gave the pure α-isomer, m. p. and mixed m. p. 232—234°.

(ii) Fractions containing glucurone and glucuronic acid were combined to give barium glucuronate (0·12 g.), chromatographically identical (solvents *b*, *f*) with authentic material.

(iii) An aldobiouronic acid (0·12 g.) which responded weakly to the *p*-anisidine spray reagent, giving a dull pink-brown stain, had R_{gal} 0·70, 0·75 (solvents *b*, *f*), and on hydrolysis with N-sulphuric acid at 98° for 9 hr. gave galactose and a uronic acid (pink stain with *p*-anisidine) with R_{gal} 1·8, 1·2 (solvents *b*, *f*).

A portion of the barium salt was de-ionised with Amberlite IR-120 (H) resin, giving the free acid (6·3 mg.) which was then heated under reflux in 1% methanolic hydrogen chloride for 7 hr. The neutralised (diazomethane) product was reduced in water (0·5 c.c.) with sodium borohydride (30 mg.) overnight, de-ionised with mixed ion-exchange resins, and hydrolysed with N-sulphuric acid at 100° for 5 hr. The products of hydrolysis corresponded (paper chromatography) to galactose and 4-*O*-methylglucose. The aldobiouronic acid may tentatively be regarded, therefore, as composed of 4-*O*-methyl-D-glucuronic acid and D-galactose units.[37]

(iv) A second aldobiouronic acid (0·60 g.) had $[\alpha]_D^{25}$ −31° (*c* 1·0), R_{gal} 0·50, 0·55 (solvents *b*, *f*), M_g 0·85, equiv. 372, and was chromatographically and ionophoretically identical with (2-D-mannose β-D-glucopyranosid)uronic acid obtained from *Hakea acicularis* gum.[20d] Heating a portion with N-sulphuric acid at 98° for 10 hr. gave glucuronic acid and mannose, with a considerable amount of unchanged material. Methylation of the aldobiouronic acid by the methods of Haworth and of Purdie afforded, after recrystallization from light petroleum (b. p. 30—60°) containing a little ether and then from ether, *methyl* (*methyl* 3,4,6-*tri*-O-*methyl*-2-D-*mannoside* 2,3,4-*tri*-O-*methyl*-β-D-*glucosid*)*uronate* as prismatic needles, m. p. 141°, $[\alpha]_D$ −22° (*c* 2·4 in MeOH) (Found: C, 51·2; H, 7·8. $C_{20}H_{36}O_{12}$ requires C, 51·3; H, 7·7%).

Hydrolysis of the fully methylated compound with 2N-sulphuric acid at 100° for 16 hr. gave two materials: (*a*) A neutral methylated sugar chromatographically identical with 3,4,6-tri-*O*-methyl-D-mannose crystallized from ether–light petroleum (b. p. 30—60°) on being nucleated, had m. p. and mixed m. p. 102—104°, $[\alpha]_D^{28}$ +40° (*c* 1·0 in MeOH), and on periodate oxidation gave a product whose chromatographic behaviour (solvents *a*, *i*) corresponded to that of 2,3,5-tri-*O*-methylarabinose. (*b*) An acid component travelled at the same rate as

[37] Cf. Abdel Akher, Smith, and Spriestersbach, *J.*, 1952, 3637; Jones and Nunn, *J.*, 1955, 3001.

2,3,4-tri-*O*-methyl-D-glucuronic acid (solvents *b*, *f*) on paper chromatograms and had $[\alpha]_D^{20}$ *ca.* +10° (*c* 1·0 in MeOH); conversion into the methyl ester methyl glycosides followed by treatment with methanolic ammonia gave a product which when dissolved in a little ethanol and nucleated with methyl 2,3,4-tri-*O*-methyl-α-D-glucosiduronamide formed elongated prisms, m. p. and mixed m. p. 188° (from ethanol–ether).

(v) A third aldobiouronic acid was obtained as barium salt (0·27 g.), slightly contaminated with a slower-moving component (see below) which responded very weakly to the *p*-anisidine spray reagent. The major component, $[\alpha]_D^{25}$ −3° (*c* 1·8), had R_{gal} 0·25, 0·35 (solvents *b*, *f*), M_g 1·0, equiv. 380; a portion gave galactose and glucuronic acid with traces of mannose on hydrolysis. The aldobiouronic acid moved at the same rate on paper chromatography and paper ionophoresis as (6-D-galactose β-D-glucopyranosid)uronic acid from *Acacia karroo* gum.[21f] Methylation in the usual way gave a fully methylated syrup which did not crystallize. Distillation of the methylated material gave a syrup which on hydrolysis by 2N-sulphuric acid at 98° for 16 hr. gave two major components, corresponding chromatographically to 2,3,4-tri-*O*-methyl-D-galactose and 2,3,4-tri-*O*-methyl-D-glucuronic acid, with a trace of material resembling 3,4,6-tri-*O*-methyl-D-mannose. The 2,3,4-tri-*O*-methyl-D-galactose, $[\alpha]_D^{20}$ +105° (*c* 3·1), was separated on thick filter-paper sheets (solvent *i*) and identified by conversion into 2,3,4-tri-*O*-methyl-*N*-phenyl-D-galactosylamine, m. p. and mixed m. p. 168—169°, $[\alpha]_D^{20}$ −70° ⟶ +45° (2 days, equil.) (*c* 1·0 in MeOH). The acidic fraction was characterized as before (previous paragraph) by conversion into the methyl ester methyl glycosides, $[\alpha]_D^{20}$ +50° (*c* 5·9 in MeOH), and thence into methyl 2,3,4-tri-*O*-methyl-α-D-glucosiduronamide, m. p. and mixed m. p. 187—188°. The mother liquors from the amide were re-hydrolyzed and shown to contain a little slower-moving acidic material and unhydrolyzed partly methylated aldobiouronic acid (tested by further hydrolysis) as well as 2,3,4-tri-*O*-methyl-D-glucuronic acid.

The residue, left after distillation of the syrupy methylated aldobiouronic acid, gave on hydrolysis 2,3,4-tri-*O*-methylglucuronic acid, a trace of 2,3,4-tri-*O*-methylgalactose, and 3,4,6-tri-*O*-methylmannose, together with a slightly faster-moving compound (solvents *b*, *i*). The two latter components were readily separated into approximately equal fractions by paper ionophoresis, 3,4,6-tri-*O*-methyl-D-mannose having M_g 0·45, and an immobile fraction.

(vi) The next fraction (0·17 g.) gave a faint pink stain with the *p*-anisidine spray reagent and had R_{gal} 0·12, 0·25 (solvents *b*, *f*), M_g 0·90. Heating a portion with N-sulphuric acid at 98° for 10 hr. gave substances corresponding on paper chromatography to (2-D-mannose β-D-glycopyranosid)uronic acid, mannose, and glucuronic acid with a barely detectable trace of galactose. After reduction with sodium borohydride followed by acid hydrolysis, mannitol was the sole glycitol detected by chromatography (solvents *d*, *j*).

(vii) The following fraction (0·39 g.) gave a brown stain with *p*-anisidine and had R_{gal} 0·05, 0·15 (solvents *b*, *f*), M_g 0·8. Partial acid hydrolysis gave the aldobiouronic acids (2-D-mannose β-D-glucopyranosid)uronic acid and (6-D-galactose β-D-glucopyranosid)uronic acid together with mannose and galactose.

(viii) Residues (0·6 g.) washed from the column could not be separated into distinct components by paper chromatography and were not further investigated.

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963. *Anhydrides of Organophosphorus Acids. Part II.* The Synthesis of Tri- and Tetra-alkyl Esters of Phosphorous Phosphoric Anhydride.*

By J. Michalski, T. Modro, and A. Zwierzak.

A convenient method of preparing tri- and tetra-alkyl esters of phosphorous phosphoric anhydride is described.

The esters of phosphorous phosphoric anhydride are of considerable interest but, since they have been difficult to prepare, little is known about them. As yet, synthesis of an anhydride of type (I) has been reported only by Corby, Kenner, and Todd [1] who have shown that *O*-benzylphosphorous *OO*-diphenylphosphoric anhydride is formed by condensation of diphenyl phosphorochloridate and benzyl hydrogen phosphite in the presence of pyridine. They were unable to obtain this compound in pure state, but they applied it successfully *in situ* as a convenient phosphorylating agent.

(I) $(RO)_2PO{\cdot}O{\cdot}PHO{\cdot}OR'$ $(RO)_2PO{\cdot}O{\cdot}P(OR')_2$ (II)

The first attempts [2] to synthesize an ester (II) were based on the action of alkyl halides on the silver salt of hypophosphoric acid, and failed. Miłobędzki and Walczyńska [3] were also unsuccessful in their efforts to prepare anhydrides (II) by treating sodium dialkyl phosphates and phosphites with dialkyl phosphorochloridites and phosphorochloridates, respectively, probably owing to difficulties in purifying the products.

Authentic tetraethyl and tetrapropyl esters of phosphorous phosphoric anhydride were first reported by A. E. and B. A. Arbuzov.[4] Produced in minute yield together with many other products of the reaction between bromine and sodium dialkyl phosphites, the substances were isolated by tedious fractional distillation. There are reports [5] that small amounts of the esters (II) are formed as a by-product in other reactions, but there is no general method for their synthesis.

We find that pure tri- and tetra-alkyl esters of phosphorous phosphoric anhydride are relatively easy to prepare. We obtained a number of them of type (I) by condensing diethyl phosphorochloridate with alkyl hydrogen phosphites in the presence of 2,6-lutidine in benzene at 35°: $(RO)_2POCl + R'O{\cdot}PHO{\cdot}OH \longrightarrow (I) + HCl$. Tetra-alkyl esters of type (II) were prepared similarly from dialkyl phosphorochloridites and dialkyl hydrogen phosphates in the presence of pyridine in benzene at 0—5°.

The reactions were smooth, but for good yields pure starting materials were needed.

Properties of our products are tabulated. At >100°, particularly in the presence of impurities, compounds of type (I) tend to decompose. Their structures seem evident from the mode of formation and infrared spectra (also from their behaviour with water, alcohols, amines, and acids which will be reported later). *O*-Ethylphosphorous *OO*-diethylphosphoric anhydride has absorption maxima (as liquid film) at 2329 (P–H), 1270 (P=O), 937, 965 (P–O–P), and 1012 cm.$^{-1}$ (P–O–Et).

From these investigations emerged the need for a more efficient method for the preparation of dialkyl phosphorochloridites. These are usually obtained by the method of Cook *et al.*,[6] in which a mixture of alcohol and tertiary amine (2 mol. of each) is added to ethereal

* Part I, *Roczniki Chem.*, 1961, **35**, 619.

[1] Corby, Kenner, and Todd, *J.*, 1952, 3669.
[2] Sänger, *Annalen*, 1886, **232**, 1; Rosenheim, Stadler, and Jacobsohn, *Ber.*, 1906, **39**, 2837; Rosenheim and Pritze, *Ber.*, 1908, **41**, 2708.
[3] Miłobędzki and Walczyńska, *Roczniki Chem.*, 1928, **8**, 486.
[4] A. E. Arbuzov and B. A. Arbuzov, *Zhur. obshchei Khim.*, 1932, **2**, 345; B. A. Arbuzov and Razumov, *ibid.*, 1937, **7**, 1762.
[5] Steinberg, *J. Org. Chem.*, 1950, **15**, 637; Kosolapoff, U.S.P. 2,503,204; Arbuzov and Balitova, *Doklady Akad. Nauk S.S.S.R.*, 1952, **83**, 577.
[6] Cook, Ilett, Saunders, Stacey, Watson, Wilding, and Woodcock, *J.*, 1949, 2921.

TABLE 1.

Trialkyl esters (I) of phosphorous phosphoric anhydride.

		Yield		Found (%)					Required (%)		
R	R′	(%)	B. p./0·005 mm.	n_D^{20}	C	H	P	Formula	C	H	P
Et	Et	51	85—86°	1·4225	29·4	6·5	25·1	$C_6H_{15}O_6P_3$	29·3	6·5	25·2
Et	Pr^n	51	88—89	1·4235	32·5	6·8	23·8	$C_7H_{17}O_6P_3$	32·3	6·9	23·8
Et	Pr^i	59	81—82	1·4240	32·4	7·1	23·6	$C_7H_{17}O_6P_3$	32·3	6·9	23·8
Et	Bu^n	52	88—89	1·4230	35·0	7·2	22·7	$C_8H_{19}O_6P_3$	35·0	7·3	22·6
Et	CH_2Ph	45	91—92	1·4574	43·3	6·3	19·9	$C_{11}H_{17}O_6P_3$	42·9	5·8	20·1
Et	Allyl	52	86—87	1·4248	32·6	6·3	23·7	$C_7H_{15}O_6P_3$	32·6	6·2	24·0

TABLE 2.

Tetra-alkyl esters (II) of phosphorous phosphoric anhydride.

		Yield		Found (%)					Required (%)		
R	R′	(%)	B. p./mm.	n_D^{25}	C	H	P	Formula	C	H	P
Et	Et	70	74°/0·01	1·4254	35·0	7·2	22·6	$C_8H_{20}O_6P_2$	35·0	7·35	22·6
Pr^n	Et	77	84—85°/0·001	1·4277	39·65	7·9	20·6	$C_{10}H_{24}O_6P_2$	39·7	8·0	20·5
Pr^n	Bu^n	78	114—115°/0·001	1·4342	47·6	9·0	17·2	$C_{14}H_{32}O_6P_2$	46·9	9·0	17·3
Pr^i	Pr^i	53	106—108°/0·15	1·4186	42·8	8·95	17·9	$C_{12}H_{28}O_6P_2$	43·6	8·5	18·75
Bu^n	Bu^n	70	106—107°/0·005	1·4341	49·7	9·4	15·3	$C_{16}H_{36}O_6P_2$	49·7	9·4	16·0
CH_2Ph	Et	88 *	—	1·5206	52·9	5·75	15·1	$C_{18}H_{24}O_6P_2$	54·3	6·1	15·55

* Crude product.

phosphorus trichloride. We have found that by adding successively pyridine (1 mol.), a mixture of alcohol and diethylaniline (1 mol. of each), and finally alcohol (1 mol.) to a benzene solution of phosphorus trichloride (1 mol.), dialkyl phosphorochloridites can be obtained in 60—70% yields, *i.e.*, double those in the method used hitherto. The products are pure and virtually free from trialkyl phosphites. The order in which amines and alcohol have to be added suggests that formation of an intermediate pyridine–phosphorus trichloride complex is an important step in this reaction.

EXPERIMENTAL

Preparation of Dialkyl Phosphorochloridites.—To phosphorus trichloride (1·0 mole) in benzene (750 ml.) pyridine (1·0 mole) was added in about 20 min. at −5° to 0° with cooling and stirring. The solution was stirred at 0° for 15 min., then a mixture of diethylaniline (1·0 mole) and the required alcohol (1·0 mole) was added during 15 min. at 0—5°. After 15 min. the second mole of alcohol was added at 0—10°. The resulting mixture was stirred for 1·5 hr. at 10—15°, then filtered, and the precipitate was washed with benzene (300 ml.). Benzene was removed at 30—40° under reduced pressure and the products were purified by distillation *in vacuo*.

The following dialkyl phosphorochloridites were prepared: diethyl (59%), b. p. 53·5—54·5°/25 mm., n_D^{20} 1·4370 (lit.,[7] 63—65°/30 mm., 1·4350); dipropyl (60%), b. p. 80°/17 mm., n_D^{20} 1·4426 (lit.,[8] 65·5—66·5°/8 mm., 1·4420); dibutyl (73%), b. p. 115—117°/25 mm., n_D^{20} 1·4454 (lit.,[9] 100—103°/12—14 mm., 1·4455); *di-isopropyl* (49%), b. p. 62—64°/12 mm., n_D^{20} 1·4242 (Found: C, 39·0; H, 7·6; P, 16·85. $C_6H_{14}ClO_2P$ requires C, 39·0; H, 7·6; P, 16·8%).

Preparation of Alkyl Hydrogen Phosphites.—Sodium ethyl, propyl, isopropyl, and butyl hydrogen phosphites were prepared as described by Nylen,[10] by the action of 1 mol. of sodium hydroxide on 1 mol. of the corresponding dialkyl phosphite in water–ethanol (1 : 1). This method was also used for preparing the sodium allyl hydrogen phosphite; the crude product (91·5%) had m. p. 180—185° (Found: P, 22·0. Calc. for $C_3H_6NaO_3P$: P, 21·5%). Ammonium benzyl hydrogen phosphite was prepared as described by Christie *et al.*[11] (71·5%; m. p. 153—154°).

The alkyl dihydrogen phosphites were prepared as follows: Dry hydrogen chloride was

[7] A. E. Arbuzov and B. A. Arbuzov, *Ber.*, 1932, **65**, 195.
[8] B. A. Arbuzov and Razumov, *Zhur. obshchei Khim.*, 1937, **7**, 1762.
[9] Gerrard, Isaacs, Machell, Smith, and Wyvill, *J.*, 1953, 1920.
[10] Nylen, *Svensk kem. Tidskr.*, 1936, **48**, 2.
[11] Christie, Elmore, Kenner, Todd, and Weymouth, *J.*, 1953, 2947.

passed through the suspension of sodium alkyl hydrogen phosphite (0·4 mole) in benzene (250 ml.) for 30 min. at 10—20° with cooling and stirring. The excess of hydrogen chloride was removed under reduced pressure, and sodium chloride was separated by means of a centrifuge and washed with benzene (*ca.* 200 ml.). The solvent was evaporated under reduced pressure and the crude alkyl dihydrogen phosphites were used for the condensations. The following alkyl dihydrogen phosphites were prepared: ethyl (91%), n_D^{20} 1·4230; propyl (67%), n_D^{20} 1·4257; isopropyl (95%), n_D^{20} 1·4211; butyl (95%), n_D^{20} 1·4292; allyl (98%), n_D^{20} 1·4390; benzyl (94%), n_D^{25} 1·5278.

Dialkyl hydrogen phosphates were prepared by Toy's method.[12] Diethyl phosphorochloridate was prepared as described by Fiszer and Michalski.[13]

O-Alkylphosphorous OO-Diethylphosphoric Anhydrides.—To diethyl phosphorochloridate (0·15 mole) and the alkyl dihydrogen phosphite (0·15 mole) in benzene (100 ml.) 2,6-lutidine (0·15 mole) in benzene (10 ml.) was added dropwise in 15 min. at 30—35° with cooling and stirring. The mixture was stirred at room temperature for 15 min. and left overnight in a refrigerator. 2,6-Lutidine hydrochloride (80—90%) was then filtered off and washed with benzene (100 ml.). After removal of benzene under reduced pressure the *anhydrides* were purified by distillation *in vacuo*. They are described in Table 1.

Preparation of Tetra-alkyl Phosphorous Phosphoric Anhydrides.—To the solution of dialkyl hydrogen phosphate (0·2 mole) and pyridine (0·2 mole) in benzene (200 ml.) the dialkyl phosphorochloridite (0·2 mole) was added dropwise in 30 min. at 0—5° with cooling and stirring. The mixture was stirred at room temperature for 1 hr., then pyridine hydrochloride (90—95%) was filtered off and washed with benzene (100 ml.). Benzene was removed under reduced pressure and the *anhydrides* were purified by distillation *in vacuo*. They are described in Table 2.

OO-Diethylphosphorous *OO*-dibenzylphosphoric anhydride could not be distilled; when it was heated above 150° violent decomposition was observed.

OO-Diethylphosphorous *OO*-diethylphosphoric anhydride was also prepared as follows. To a suspension of sodium diethyl phosphate (20·3 g.) in benzene (140 ml.) diethyl phosphorochloridite (18·0 g.) was added at 3—5° with cooling and stirring. The mixture was then stirred at 20° for 2 hr. and sodium chloride was removed by use of a centrifuge. After removal of benzene under reduced pressure distillation gave the tetraethyl ester of phosphorous phosphoric anhydride (18·0 g., 57%), b. p. 78—80°/0·05 mm., n_D^{20} 1·4269.

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[12] Toy, *J. Amer. Chem. Soc.*, 1948, **70**, 3882.
[13] Fiszer and Michalski, *Roczniki Chem.*, 1952, **26**, 688.

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964. *Activity Coefficients of Non-electrolytes in Aqueous Solutions of Sugars.*

By A. Graham Foster and I. R. Siddiqi.

Solubility and partition methods have been used to determine activity coefficients of quinol and of ethyl butyrate in aqueous solutions of various sugars. Both " salting-out " and " salting-in " effects have been observed, which follow the well-known Setchenow equation with numerical coefficients of the same order of magnitude as was found for electrolytes.

Although the phenomenon of " salting-out " has been extensively investigated during the past fifty years,[1] little attention has been paid to the effects of organic substances,

[1] Rothmund, " Löslichkeit und Löslichkeitsbeeinflussung," Barth, Leipzig, 1907; Euler, *Z. phys. Chem.*, 1904, **49**, 303. Euler and Svanberg, *Z. Elektrochem.*, 1917, **23**, 192; Eyre, *Brit. Ass. Reports*, 1910, 425; 1912, 795; Randall and Failey, *Chem. Rev.*, 1927, **4**, 271, 285, 291; Scatchard, *ibid.*, **3**, 383; *Trans. Faraday Soc.*, 1927, **23**, 454; Gross, *Chem. Rev.*, 1937, **13**, 91; Albright, *J. Amer. Chem. Soc.*, 1937, **59**, 2098; Long and McDevit, *Chem. Rev.*, 1952, **51**, 119.

such as sugars, on the solubility of other organic compounds in aqueous solution. From the few examples available [2] it appears that sucrose, like salt, decreases the solubilities of esters in water. In the present work we examined this feature by following the solubilities of ethyl butyrate and of quinol in various sugar solutions.

Experimental.—Ethyl butyrate. Saturated solutions of ethyl butyrate in water and in sugar solutions of differing molality were prepared by shaking 50 ml. of solvent with 1 ml. of ester in glass-stoppered bottles immersed in a thermostat at 25° for periods up to 12 hr. Aliquot parts (3 ml.) were made up to 100 ml. with di-isopropyl ether and shaken at intervals for 2 hr.; then 5 ml. of the clear ether extract were removed for analysis, leaving behind the sugaring-out agent.

The ester was determined colorimetrically by a method due to Feigl [3] and Thompson,[4] based on the formation in alkaline solution of hydroxamic acids which form red complexes with ferric iron. Hydroxylamine reagent was prepared freshly before use by mixing equal volumes of methanol solutions of hydroxylamine hydrochloride (5%) and sodium hydroxide (12·5%); the precipitated sodium chloride was filtered off. A ferric perchlorate reagent was prepared by dissolving iron (0·4 g.) or hydrated ferric chloride (1·93 g.) in concentrated hydrochloric acid (5 ml.), adding 70% perchloric acid (5 ml.) and evaporating the solution, the residue being then dissolved in water and made up to 100 ml. To 10 ml. of this stock solution were added 70% perchloric acid (37·5 ml.) and ethanol (400 ml.), alternately in small amounts with cooling; this mixture was then made up to 500 ml. at room temperature.

The ethereal solution of the ester (5 ml.) was mixed with the hydroxylamine reagent (1·5 ml.) in small tubes with ground-glass stoppers. After 30 min. at 25°, ferric perchlorate reagent (12·5 ml.) was added and the whole shaken. After 10 min., the optical density at 520 mμ was read against a reagent control in 1 cm. closed silica cells, in a Hilger spectrophotometer. A calibration curve enabled ester concentrations to be calculated.

Quinol. Quinol was twice recrystallised from hot acetone. 50 ml. of a 0·05M-solution of quinol in di-isopropyl ether were shaken with 50 ml. of water or of the appropriate sugar solution in glass-stoppered bottles for 4—6 hr. in a thermostat at 25°, then left until the two layers had separated, after which 10 ml. portions of each layer were withdrawn and the quinol contents determined by titration with ceric sulphate with ferroin as indicator.

Results.—The solubility (s^0) of ethyl butyrate in water at 25° was found to be 1·76 g. l.$^{-1}$. Table 1 records the solubilities at varying molalities of sugars and other substances together

TABLE 1.

	Sucrose		Glucose		Fructose		Sorbitol	
m	$10s$	$\log_{10} f$	$10s$	$\log_{10} f$	$10s$	$\log_{10} f$	$10s$	$\log_{10} f$
0·25	1·54	0·058	1·65	0·028	1·66	0·025	—	—
0·50	1·40	0·099	1·47	0·078	1·49	0·072	1·46	0·081
1·00	1·06	0·220	1·24	0·152	1·29	0·135	1·19	0·170
2·00	0·68	0·413	0·80	0·342	0·90	0·291	0·80	0·342
k	0·206		0·167		0·146		0·163	

	Glycerol		Sodium chloride		Lactose			Maltose	
m	$10s$	$\log_{10} f$	$10s$	$\log_{10} f$	m	$10s$	$\log_{10} f$	$10s$	$\log_{10} f$
0·50	1·73	0·0095	1·40	0·100	0·125	1·70	0·015		
1·00	1·64	0·031	1·05	0·234	0·250	1·59	0·044		
2·00	1·59	0·044	0·63	0·446	0·375	—		1·55	0·055
4·00	1·33	0·122	0·21	0·923	0·500	1·30	0·132		
					0·75	—		1·21	0·163
					1·50	—		0·77	0·359
	0·032		0·234			0·270		0·240	

Glasstone and Pound [2] obtained the following k values for ethyl acetate: lactose, 0·25; sucrose, 0·216; glucose, 0·16; fructose, 0·132.

[2] Glasstone and Pound, *J.*, 1925, **125**, 2660; Glasstone, Dimond, and Harris, *J.*, 1927, 2939; Philip, and Bramley, *J.*, 1915, **107**, 377; Sugden, *J.*, 1926, 175.

[3] Feigl, "Quantitative Analysis by Spot Tests," Elsevier, 3rd edn., 1946, p. 538.

[4] Thompson in Steyermark's "Quantitative Organic Microanalysis," Blakiston, N.Y., 1951, p. 244.

with the corresponding values of $\log f = \log s^0/s = km$, where m is the sugar molality and k is Setchenow's salting-out coefficient.[5] Corresponding results for quinol are given in Table 2. Most of the results give a fairly good linear plot of $\log f$ against molality of sugar, for which the values of k have been calculated. The partition coefficient of quinol between di-isopropyl ether and water at 25° was found to be $C_{H_2O}/C_{ether} = 1{\cdot}35$.

Discussion.—The salting-out coefficients for ethyl butyrate vary over a wide range and some sugars, *viz.*, lactose and maltose, are even more effective than sodium chloride. The effect of some sugars on the solubility of ethyl acetate was studied by Glasstone and Pound [2] who expressed their results in terms of " hydration numbers." These data have been converted into activity coefficients and the salting-out coefficients derived therefrom (listed in Table 1) lie very close to the values obtained in the present work with ethyl butyrate.

TABLE 2.

	Cellobiose		Erythritol		Galactose		Glucose		Lactose		Maltose	
m	P	$\log f$	P	$\log f$	P	$\log f$	P	$\log f$	P	$\log f$	P	$\log f$
0·125	1·38	−0·007							1·39	−0·010		
0·25	1·41	−0·015	1·376	−0·007			1·34	0·005	1·42	−0·020		
0·375					1·37	−0·004					1·44	−0·026
0·50	1·45	−0·030	1·381	−0·009			1·32	0·012	1·48	−0·039		
0·75					1·38	−0·007					1·53	−0·051
1·0			1·403	−0·015			1·29	0·023				
1·5					1·41	−0·017					1·69	−0·095
2·0			1·447	−0·029			1·22	0·048				
k	−0·06		−0·013		−0·011		0·026		−0·076		−0·062	

	Mannitol		Me α-Glucoside		Rhamnose		Sorbitol		Sucrose	
m	P	$\log f$	P	$\log f$	P	$\log f$	P	$\log f$	P	$\log f$
0·25	1·34	0·005	1·41	−0·021	1·39	−0·008				
0·50	1·32	0·010	1·47	−0·039	1·42	−0·018	1·33	0·009	1·34	0·014
0·75	1·29	0·020					1·31	0·013		
1·0			1·61	−0·079	1·48	−0·036	1·30	0·017	1·31	0·025
1·5									1·27	0·036
2·0			1·97	−0·167	1·59	−0·067	1·24	0·039	1·24	0·047
k	0·021		−0·084		−0·036		0·017		0·024	

Glycerol			Pentaerythritol			Sodium chloride		
m	P	$\log f$	m	P	$\log f$	m	P	$\log f$
0·55	1·44	0·0186	0·075	1·39	−0·011	0·5	1·148	0·074
0·82	1·47	0·0287	0·15	1·42	−0·020	1·0	0·971	0·146
1·53	1·58	0·0605	0·30	1·46	−0·34	2·0	0·714	0·279
2·18	1·70	0·0916				4·0	0·386	0·547
4·15	2·09	0·1817						
k	0·048			−0·100			0·133	

Table 2 reveals the existence of " salting-in " effects of the same order of magnitude as the salting-out effects. Comparison with Table 1 shows that there is no correlation between the effects of given sugars on ethyl butyrate and on quinol. Lactose and maltose, which have the largest positive values of k with ethyl butyrate, have negative values with quinol. It is not yet possible to correlate these effects with the structures of the sugars and discussion must be deferred.

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[*Received, June 9th*, 1961.]

[5] Setchenow, *Z. phys. Chem.*, 1889, **4**, 117.

965. *Aminoditolylborane and the Preparation of Diarylborinic Acids.*

By G. E. Coates and J. G. Livingstone.

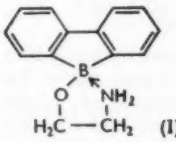
Aminodi-*o*-tolyl- and aminodimesityl-borane are monomeric in benzene solution, dimerization being prevented sterically by the *o*-methyl groups. The reaction between dichlorodiphenylaminoborane and an aryl Grignard reagent appears to be the best general method for the preparation of diarylborinic acids, which have been obtained as 2-aminoethyl esters in 51—93% yields.

Aminodiarylboranes, $Ar_2B{\cdot}NR_2$, have hitherto [1,2] been found to be dimeric when R = H, monomeric when R is an alkyl or aryl group, and both mono- and di-meric forms of $Ph_2B{\cdot}NHMe$ have been obtained.[3] We suggested [1] that in dimeric aminodiarylboranes $Ar_2B{\cdot}NR_2)_2$ any groups R bigger than hydrogen would cause substantial steric interference even with the hydrogen atoms in *ortho*-positions on the aryl groups. We now find that substitution of one or both *o*-hydrogen atoms by methyl groups also prevents dimerization; both aminodi-*o*-tolylborane and aminodimesitylborane are monomeric in benzene solution. Their dipole moments are small, being respectively $\mu = 1{\cdot}7$ and *ca.* 1·1 D. The moment of fluorodimesitylborane (1·7 D) is significantly smaller than that of chlorodiphenylborane (2·0 D), and we attribute part of the difference to the prevention of overlap between the boron 2*p*-orbital and the mesityl π-orbitals on account of the steric requirements of the mesityl groups.

The quantitative hydrolysis of aminodiarylboranes to diarylborinic acids, the simple preparation of the former from aminodichloroboranes ($Cl_2B{\cdot}NR_2$; R = alkyl or aryl) and a Grignard reagent,[2] and the easy preparation of dichlorodiphenylaminoborane from diphenylamine and trichloroborane,[4] lead us to consider the following reaction sequence the best preparative route to diarylborinic acids:

$$BCl_3 \xrightarrow{Ph_2NH} Cl_2B{\cdot}NPh_2 \xrightarrow{ArMgX} Ar_2B{\cdot}NPh_2 \xrightarrow{H_2O\text{–}NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH} Ar_2B{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2 \xrightarrow{HCl} Ar_2B{\cdot}OH$$

Since only a slight excess of Grignard reagent is used, this procedure is more economical than that of Povlock and Lippincott [5] in which a 50% excess of Grignard reagent is allowed to react with trimethoxyboroxine, and the yield of 2-aminoethyl diarylborinate is then only 21—63% (based on the boroxine) and some boronic acid is formed as well. By our method, yields of 2-aminoethyl esters have been in the range 51—93%, and boronic acids have never been detected among the products. The method was also used for the preparation of 2-aminoethyl biphenyl-2,2′-borinate (I).



(I)

Experimental

The preparation of diphenylborinic acid and its 2-aminoethyl ester, described below, illustrates the general method used for the preparation of the compounds listed in the Table.

2-Aminoethyl Diphenylborinate.—Phenylmagnesium bromide (0·25 mole) in ether was slowly added to dichlorodiphenylaminoborane [4] (0·1 mole) in benzene (100 c.c.). After the mixture had been refluxed for ½ hr., it was allowed to cool, then hydrolysed with dilute hydrochloric acid, and the pH adjusted to 6—7. After filtration the organic phase was evaporated, the residual yellow oil consisting of crude diphenylborinic acid was dissolved in ether (50 c.c.)

[1] Coates and Livingstone, *J.*, 1961, 1000.
[2] Niedenzu and Dawson, *J. Amer. Chem. Soc.*, 1959, **81**, 5553.
[3] Mikhailov and Fedotov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1959, 1482.
[4] Becher, *Z. anorg. Chem.*, 1957, **289**, 277.
[5] Povlock and Lippincott, *J. Amer. Chem. Soc.*, 1958, **80**, 5409.

and 2-aminoethanol (22 c.c.) in an equal volume of water was added with stirring. The precipitated ester was separated from any residual diphenylamine by crystallization from ethanol; it (22·6 g.) had m. p. 188—189° (lit.[5] 189°).

Diphenylborinic Acid.—The 2-aminoethyl ester (22·6 g.) in a mixture of acetone (50 c.c.) and methanol (50 c.c.) was hydrolysed by addition of hydrochloric acid (12·5 c.c. of concentrated acid in 100 c.c. of water). After addition of ether (100 c.c.) the organic layer was separated, dried ($MgSO_4$), and evaporated, yielding diphenylborinic acid (16·1 g.), b. p. 210—213°, condensing as anhydride, m. p. 116° (from hexane) (lit.,[6] 116°).

Preparation of diarylborinic esters and acids, $R_2B{\cdot}OR'$.

	Ester, R′ = ·$CH_2{\cdot}CH_2{\cdot}NH_2$						Acid, R′ = H					
		Yield	Found (%)		Reqd. (%)			Yield	Found (%)		Reqd. (%)	
R	M. p.	(%)	C	H	C	H	M. p.	(%)	C	H	C	H
C_6H_5	188—189°	93	74·1	7·1	74·6	7·2	Liquid	88	78·9	6·0	79·2	6·1
o-$CH_3{\cdot}C_6H_4$	184	80	76·1	7·9	75·9	7·9	78—79°	75	79·9	7·1	80·1	7·2
p-$CH_3{\cdot}C_6H_4$	186	80	75·4	7·0	75·9	7·9	105	71	78·9	7·2	80·1	7·2
o-$CH_3O{\cdot}C_6H_4$[a]	164—165	58	67·4	7·0	67·3	7·0	[b]	—	—	—	—	—
p-$Br{\cdot}C_6H_4$	236—237	56	43·3	3·6	43·8	3·7	84—86	50	42·0	4·6	42·4	4·6
p-$Cl{\cdot}C_6H_4$	226—227	82	56·8	4·6	57·1	4·8	77	75	57·0	3·5	57·4	3·6
p-$C_6H_5{\cdot}C_6H_4$	219	57	81·9	6·4	82·8	6·4	[b]	—	—	—	—	—
1-$C_{10}H_7$	204	51	80·9	6·1	81·2	6·2	117	45	84·7	5·1	85·0	5·3
$C_6H_5{\cdot}C{\equiv}C$[a]	172—174	58	78·8	7·1	79·1	7·4	98—100	52	83·3	4·6	83·4	4·8
3,4-$(CH_3)_2C_6H_3$[a]	204—206	72	76·1	8·4	76·8	8·6	[b]	—	—	—	—	—

[a] Not previously described. [b] Acids were prepared only when needed for further study.

Aminodi-o-tolylborane.—Chlorodi-*o*-tolylborane (4·5 g., 0·02 mole; b. p. 100—102°/0·01 mm., prepared from di-*o*-tolylborinic acid and boron trichloride[6]) in ether was slowly added to a solution of ammonia (about 0·5 g.) and triethylamine (2·1 g.) in ether (100 c.c.) at about −40°. There was an immediate white precipitate. The mixture was refluxed for ½ hr., then filtered from triethylammonium chloride. Vacuum-distillation yielded a colourless liquid *product* 2·93 g., b. p. 86—88°/$<10^{-3}$ mm. (Found by hydrolysis: *o*-$tolyl_2B$, 91·9; NH_2, 7·6, 7·4. $C_{14}H_{16}BN$ requires *o*-$tolyl_2B$, 92·3; NH_2, 7·7%).

Aminodimesitylborane.—Fluorodimesitylborane[7] (6 g.) in ether (50 c.c.) was slowly added to an excess of anhydrous ammonia in ether (50 c.c.). There was immediate precipitation of the borane–ammonia complex. The mixture was refluxed for 48 hr., during which the ammonia complex gradually dissolved and ammonium fluoride (0·4 g.) was deposited. The ether solution was filtered and evaporated, yielding aminodimesitylborane (5·5 g., 93%), m. p. 118—120° (from light petroleum) {Found by hydrolysis: $[(CH_3)_3C_6H_2]_2B$, 93·4, 93·5; NH_2, 5·96, 5·92. $C_{18}H_{24}BN$ requires $[(CH_3)_3C_6H_2]_3B$, 94·1; NH_2, 6·0%)}.

2-Aminoethyl Biphenyl-2,2′-borinate (I).—n-Butyl-lithium (0·08 mole) in ether was added to 2,2′-dibromobiphenyl[8] (10 g., 0·032 mole) in ether (100 c.c.), and the mixture stirred for 4 hr. before dichlorodiphenylaminoborane (0·032 mole) in dry benzene was slowly added. After addition of water (50 c.c.) the pale yellow organic layer was separated and a solution of 2-aminoethanol (10 c.c.) in water (50 c.c.) was added. The precipitated *ester*, crystallised from ethanol, had m. p. 170—171° (3·9 g., 61%) (Found: C, 75·3; H, 6·2. $C_{14}H_{14}BNO$ requires C, 75·1; H, 6·3%).

Infrared Spectra.—Both aminoboranes showed very strong absorptions at 1450 (*o*-tolyl compound) and 1419 (mesityl compound) cm.$^{-1}$ (measured in benzene solution), which we attribute to a B–N stretching vibration. These frequencies, which show the isotopic splitting commonly observed in spectra of boron compounds, are higher than those of corresponding bands in other monomeric aminodiarylboranes,[1] which lie in the range 1360—1410 cm.$^{-1}$. This is to be expected since the *o*-methyl groups would reduce interaction between the boron 2*p*-orbital and the aryl π-electrons, and this should increase the order of the B–N bond.

The N–H frequencies of the *o*-tolyl compound, measured as a contact film, were 3390 and 3490 cm.$^{-1}$.

Dipole Moments.—These were measured for benzene solutions, refractivities being measured

[6] Abel, Dandegaonker, Gerrard, and Lappert, *J.*, 1956, 4697.
[7] Brown and Dodson, *J. Amer. Chem. Soc.*, 1957, **79**, 2305.
[8] Gilman and Gaj, *J. Org. Chem.*, 1957, **22**, 447.

Aminodi-o-tolylborane

Wt. fraction (w)	Spec. volume (v)	$10^5\,\Delta n$	ΔC (cm.)
0·1668	1·1424	17·92	0·140
0·1858	1·1410	21·73	0·220
0·2802	1·1391	33·81	0·351
0·3093	1·1387	59·17	—

$dC/dw = 1·867$, $dv/dw = -0·291$, $dn/dw = 0·1034$, ${}_TP = 127·8$, ${}_EP = 64·6$, ${}_OP = 60·0$ c.c., $\mu = 1·7$ D.

Chlorodiphenylborane

0·0079	1·1419	59·57	0·174
0·0123	1·1404	93·79	0·478
0·0268	1·1367	111·5	0·940
0·0342	1·1329	119·1	1·267

$dC/dw = 2·527$, $dv/dw = -0·3425$, $dn/dw = 0·1155$, ${}_TP = 143·2$, ${}_EP = 60·3$, ${}_OP = 79·9$ c.c., $\mu = 2·0$ D.

Aminodimesitylborane

Wt. fraction (w)	Spec. volume (v)	$10^5\,\Delta n$	ΔC (cm.)
0·0676	1·1421	37·90	0·218
0·1177	1·1417	66·78	0·342
0·1698	1·1401	86·64	0·383
0·2733	1·1395	97·47	0·421

$dC/dw = 0·9771$, $dv/dw = -0·1264$, $dn/dw = 0·0799$, ${}_TP = 119·1$, ${}_EP = 90·5$, ${}_OP = 24·1$ c.c., $\mu = ca.\ 1·1$ D.

Fluorodimesitylborane

0·0045	1·1417	—	0·066
0·0102	1·1402	—	0·174
0·0143	1·1396	—	0·233
0·0257	1·1378	—	0·321

$dC/dw = 7·4861$, $dv/dw = -0·1839$, ${}_TP = 148·3$, ${}_EP$ (calc. from bond refractivities for 5893 Å) $= 84·9$, ${}_OP = 59·2$ c.c., $\mu = 1·7$ D.

at 6620 Å. Atom polarization was arbitrarily taken as 5% of the electron polarization at 6620 Å. Moments were calculated from observed weight fractions, densities, refractivities, and changes of capacity by Halverstat and Kumler's method.[9]

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[*Received, June 15th*, 1961.]

[9] Halverstat and Kumler, *J. Amer. Chem. Soc.*, 1942, **64**, 2988.

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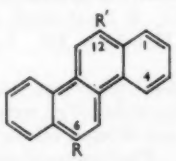
966. 12-*Benzyl-* *and* 12-*Alkyl*-6-*aminochrysenes.*

By PHILIPPE MABILLE and N. P. BUU-HOÏ.

12-Benzyl-, 12-hexyl-, and 12-heptyl-6-aminochrysene have been synthesised for biological evaluation as antileukæmia agents. Several functional derivatives of these amines and other new substituted chrysenes were also prepared.

6-HEXYLCHRYSENE (I; $n = 4$) and 6-heptylchrysene (I; $n = 5$) were readily prepared by Wolff–Kishner reduction of 6-hexanoyl- and 6-heptanoyl-chrysene by the Huang-Minlon modification;[1] these two ketones were obtained in excellent yields, and free from isomers, by Friedel–Crafts acylation of chrysene in the presence of aluminium chloride in methylene chloride. 6-Heptanoylchrysene and its reduction-product had already



(I); R = H, R′ = CH_3·$[CH_2]_n$·CH_3
(II); R = NO_2, R′ = CH_3·$[CH_2]_n$·CH_3
(III); R = NH_2, R′ = CH_3·$[CH_2]_n$·CH_3
(IV); R = NO_2, R′ = CH_2Ph
(V); R = NH_2, R′ = CH_2Ph

been prepared by Carruthers and Cook[2] by Clemmensen's method, which gave less satisfactory results. Nitration of the hydrocarbons (I) with fuming nitric acid in acetic acid gave 12-hexyl-6-nitro- (II; $n = 4$) and 12-heptyl-6-nitro-chrysene (II; $n = 5$), reduced to the corresponding amines by use of hydrazine hydrate in the presence of Raney

[1] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.
[2] Carruthers and Cook, *J.*, 1954, 2047.

nickel, a procedure which, applied to 6-nitrochrysene, was more satisfactory than that described in the literature.[3]

Nitration of 6-benzylchrysene furnished, in addition to the expected 12-benzyl-6-nitrochrysene (IV), a substance of unknown structure. Reduction of the nitro-compound (IV) was also achieved with hydrazine hydrate and Raney nickel The *meso*-position of the amino-group was confirmed by oxidation of 6-acetamido-12-benzylchrysene with chromic acid to 12-benzylchrysene-5,6-quinone, also obtained by similar oxidation of 6-benzylchrysene, the main product in this case being 12-benzoylchrysene-5,6-quinone.[4]

Condensation with hexane-2,5-dione and phenacylacetone of the three 12-substituted 6-aminochrysenes readily gave the corresponding 1-6′-chrysenyl-2,5-dimethylpyrroles and -2-methyl-5-phenylpyrroles.

Preliminary biological investigations show that the aminochrysenes (III) possess antileukæmia activity in mice, whereas the pyrroles are inactive.

Experimental

6-Hexanoylchrysene.—To anhydrous methylene chloride (500 c.c.) were added, with stirring, finely powdered aluminium chloride (18 g.), hexanoyl chloride (17·5 g.), and a suspension of chrysene [5] (22 g.) in methylene chloride (300 c.c.). The dark greenish-brown solution was left for 2 hr. at room temperature and then refluxed for 7 hr. After cooling and decomposition with ice and hydrochloric acid, the organic layer was washed with dilute aqueous sodium hydroxide and then with water, and dried ($CaCl_2$). The residue, obtained by removal of solvent, was crystallised twice from ethanol (450 c.c.), giving shiny needles (26 g., 80%), m. p. 85°, whose solutions in sulphuric acid were orange-yellow (Found: C, 88·2; H, 6·6. $C_{24}H_{22}O$ requires C, 88·3; H, 6·8%).

6-Heptanoylchrysene was similarly prepared in 80% yield, and no isomers were isolated. The product crystallised as needles, m. p. 67°, from ethanol (lit.,[2] m. p. 66°).

6-Hexylchrysene (I; $n = 4$).—A mixture of 6-hexanoylchrysene (24·5 g.), hydrazine hydrate (95%; 24 g.), potassium hydroxide (20 g.), and diethylene glycol (750 c.c.) was refluxed for 5 hr. with removal of water. Cooling, dilution with water, and acidification with hydrochloric acid gave a precipitate, which was washed with water and recrystallised from ethanol. The product (23 g., 98·3%) had m. p. 87—88° (Found: C, 92·5; H, 7·5. $C_{24}H_{24}$ requires C, 92·3; H, 7·7%).

6-Heptylchrysene (I; $n = 5$), similarly prepared and in similar yield, crystallised as needles, m. p. 86°, from ethanol (lit.,[2] m. p. 83—84°).

12-Hexyl-6-nitrochrysene (II; $n = 4$).—To a suspension of 6-hexylchrysene (15·6 g.) in acetic acid (500 c.c.), a solution of fuming nitric acid (15 c.c., d 1·4) in acetic acid (100 c.c.) was added in one portion at 45° and with stirring. The precipitate that formed on cooling was collected, washed with acetic acid, water, and finally with ethanol, and recrystallised from ethanol–acetone (2 : 1 v/v). The golden-yellow leaflets (13 g., 73%), m. p. 111°, gave no halochromy in sulphuric acid (Found: C, 80·8; H, 6·6; N, 4·1. $C_{24}H_{23}NO_2$ requires C, 80·6; H, 6·5; N, 3·9%).

12-Heptyl-6-nitrochrysene (II; $n = 5$) was prepared from 6-heptylchrysene (13·1 g.) and fuming nitric acid (14 c.c., d 1·4) in acetic acid (500 c.c.); it crystallised as yellow needles (10 g.), m. p. 107°, from ethanol–acetone (Found: C, 80·9; H, 6·5; N, 3·8. $C_{25}H_{25}NO_2$ requires C, 80·8; H, 6·8; N, 3·8%).

6-Amino-12-hexylchrysene (III; $n = 4$).—To 12-hexyl-6-nitrochrysene (10·7 g.) in benzene–ethanol (1 : 1 v/v) hydrazine hydrate (98%; 10 g.) and Raney nickel (3 g.) were added (evolution of nitrogen). After 1 hour's refluxing the Raney nickel was filtered off and the filtrate concentrated (to 250 c.c.) and left overnight in the refrigerator. The cream-coloured needles (9·7 g., 98%) crystallised from ethanol–benzene with considerable loss but furnished almost colourless needles (6 g.), m. p. 135°. These gave no halochromy in sulphuric acid and darkened on exposure to light and heat (Found: C, 88·0; H, 7·7; N, 4·4. $C_{24}H_{25}N$ requires C, 88·0; H, 7·7; N, 4·3%). *6-Acetamido-12-hexylchrysene*, prepared by refluxing for 3 min. a solution of

[3] Newman and Cathcart, *J. Org. Chem.*, 1940, **5**, 618.
[4] Funke and Ristic, *J. prakt. Chem.*, 1936, **146**, 151.
[5] Cf. Mabille and Buu-Hoï, *J. Org. Chem.*, 1960, **25**, 1937.

the foregoing amine (1·6 g.) and acetic anhydride (5 c.c.) in benzene (25 c.c.), crystallised as needles (1 g.), m. p. 215° (from toluene) (Found: C, 84·6; H, 7·2; N, 3·9. $C_{26}H_{27}NO$ requires C, 84·5; H, 7·4; N, 3·8%).

1-(12-*Hexyl*-6-*chrysyl*)-2,5-*dimethylpyrrole*.—A mixture of the corresponding amine (0·8 g.) and hexane-2,5-dione (0·8 g.) was heated at 130° for 30 min.; the brown oil obtained on cooling solidified on treatment with ethanol–acetone. Recrystallisation from ethanol furnished needles (0·3 g.), m. p. 133°, giving a yellowish-brown halochromy in sulphuric acid (Found: C, 88·9; H, 7·5; N, 3·7. $C_{30}H_{31}N$ requires C, 88·8; H, 7·7; N, 3·5%). 1-(12-*Hexyl*-6-*chrysyl*)-2-*methyl*-5-*phenylpyrrole*, similarly prepared from the amine (0·8 g.) and phenacylacetone (0·6 g.), crystallised as cream-coloured needles (0·3 g.), m. p. 138°, from ethanol, giving a yellow halochromy in sulphuric acid (Found: C, 89·7; H, 7·1; N, 3·1. $C_{33}H_{33}N$ requires C, 89·9; H, 7·1; N, 3·0%).

6-*Amino*-12-*heptylchrysene* (III; $n = 5$).—Prepared as for the lower homologue from 12-heptyl-6-nitrochrysene (9·27 g.), hydrazine hydrate (15 c.c.), and Raney nickel (3 g.), this *amine* crystallised from ethanol–benzene as needles (5·1 g.), m. p. 118°, darkening on exposure to light and heat (Found: C, 88·2; H, 7·8; N, 4·2. $C_{25}H_{27}N$ requires C, 87·9; H, 8·0; N, 4·1%).

6-*Acetamido*-12-*heptylchrysene* crystallised as prisms, m. p. 213° (acetone–benzene) (Found: C, 84·6; H, 7·6; N, 3·9. $C_{27}H_{29}NO$ requires C, 84·6; H, 7·6; N, 3·7%).

1-(12-*Heptyl*-6-*chrysyl*)-2,5-*dimethylpyrrole*.—Prepared from the amine (0·6 g.) and hexane-2,5-dione (0·7 g.), this *pyrrole* crystallised as shiny needles (0·4 g.), m. p. 128° (from ethanol) (Found: C, 88·4; H, 8·0; N, 3·5. $C_{31}H_{33}N$ requires C, 88·7; H, 7·9; N, 3·3%). 1-(12-*Heptyl*-6-*chrysyl*)-2-*methyl*-5-*phenylpyrrole*, obtained from the amine (0·6 g.) and phenacylacetone (0·8 g.), crystallised as prisms (0·1 g.), m. p. 130—131° (from acetone) (Found: C, 89·8; H, 7·0; N, 3·1. $C_{36}H_{35}N$ requires C, 89·8; H, 7·3; N, 2·9%).

Nitration of 6-*Benzylchrysene*.—To a suspension of 6-benzylchrysene (15·92 g.) in acetic acid (1 l.) at 40°, a solution of fuming nitric acid (15 c.c.) and sulphuric acid (1·5 c.c.) in acetic acid (200 c.c.) was added in one portion, with stirring. Stirring was continued for 30 min. at 40°, and after cooling, the precipitate was washed with acetic acid, then with water, giving a crude product (12 g.), m. p. 188—189°. Dilution of the filtrate with water and crystallisation from benzene yielded yellow needles (3 g.), m. p. 186—188°. The two crops were combined and crystallised, furnishing yellow prisms (12 g., 66%) of 12-*benzyl*-6-*nitrochrysene* (IV), m. p. 189°, which gave no halochromy in sulphuric acid (Found: C, 82·7; H, 4·6; N, 3·9. $C_{25}H_{17}NO_2$ requires C, 82·6; H, 4·7; N, 3·9%). Oxidation of 12-benzyl-6-nitrochrysene (3 g.) with sodium dichromate (15 g.) in acetic acid (220 c.c.) (14 hr. under reflux) afforded 12-nitrochrysene-5,6-quinone.[6]

6-*Amino*-12-*benzylchrysene* (V).—Reduction of 12-benzyl-6-nitrochrysene (5·44 g.) in ethanol (500 c.c.)–benzene (300 c.c.) by means of hydrazine hydrate (2·5 g.) and Raney nickel (3 g.) was complete after 5 hours' refluxing and gave a crude amine (4·5 g., 90%), m. p. 217°. Crystallisation from benzene gave prisms (3·3 g.), m. p. 218°. The ethanol or benzene solutions displayed a blue fluorescence, and the solutions in sulphuric acid were colourless (Found: C, 90·2; H, 5·9; N, 4·2. $C_{25}H_{19}N$ requires C, 90·1; H, 5·7; N, 4·2%). 6-*Acetamido*-12-*benzylchrysene* crystallised as short needles, m. p. 271° (from toluene) (Found: C, 86·5; H, 5·6; N, 3·6. $C_{27}H_{21}NO$ requires C, 86·4; H, 5·6; N, 3·7%).

1-(12-*Benzyl*-6-*chrysyl*)-2,5-*dimethylpyrrole*.—Prepared by refluxing for 30 min. a mixture of the corresponding amine (0·5 g.) and hexane-2,5-dione (1 g.), this *pyrrole* crystallised as cream-coloured needles (0·2 g.), m. p. 244—245°, from ethanol–benzene (Found: C, 90·2; H, 6·2; N, 3·5. $C_{31}H_{25}N$ requires C, 90·5; H, 6·1; N, 3·4%).

1-(12-*Benzyl*-6-*chrysyl*)-2-*methyl*-5-*phenylpyrrole*, obtained by heating for 20 min. at 180° a mixture of the amine (0·5 g.) and phenacylacetone, crystallised as cream-coloured needles (0·3 g.), m. p. 219—220°, from ethanol–benzene (Found: C, 91·3; H, 5·9; N, 3·0. $C_{36}H_{27}N$ requires C, 91·3; H, 5·7; N, 3·0%).

Oxidation of 6-*Acetamido*-12-*benzylchrysene*.—This compound (1 g.), sodium dichromate (3 g.), and acetic acid (85 c.c.) were refluxed for 150 min. then cooled and stored for 12 hr.; the precipitate was washed with acetic acid, and crystallised from toluene, giving 12-*benzylchrysene*-5,6-*quinone* (V) as needles (0·4 g.), m. p. 263—264° (decomp. >233—235° on prolonged heating), whose solutions in sulphuric acid were Indigo-blue (Found: C, 86·4; H, 4·7; O, 9·4. $C_{25}H_{16}O_2$

[6] Buu-Hoï, *J. Org. Chem.*, 1954, **19**, 1396.

requires C, 86·2; H, 4·6; O, 9·2%). The same compound (0·5 g.) was obtained by refluxing for 150 min. a mixture of 6-benzylchrysene (2 g.), sodium dichromate (6 g.), and acetic acid (80 c.c.). As a by-product, 12-benzoylchrysene-5,6-quinone was obtained, and characterised by its phenazine [yellowish prisms (from acetic acid), m. p. 222° (lit.,[7] m. p. 207°)], giving a violet halochromy in sulphuric acid. The *phenazine* corresponding to 12-benzylchrysene-5,6-quinone was prepared from the quinone (0·3 g.) and *o*-phenylenediamine (0·2 g.) in acetic acid; it crystallised as greenish-yellow needles (0·2 g.), m. p. 230° (from toluene), and gave, in sulphuric acid, an olive-green colour which rapidly turned blue (Found: C, 88·5; H, 4·8; N, 6·8. $C_{31}H_{20}N_2$ requires C, 88·5; H, 4·8; N, 6·7%).

This project was aided by the Institut National d'Hygiène and the Anna Fuller Fund. Our thanks are due to Professor Bugnard and to Professor William U. Gardner.

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GIF-SUR-YVETTE (SEINE-ET-OISE), FRANCE. [*Received, June 23rd,* 1961.]

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967. *The Stability of Calcium Hydrogen Phosphate Precipitated from Solutions of Calcium Nitrate and Phosphoric Acid.*

By D. H. BOOTH and R. V. COATES.

Calcium hydrogen phosphate dihydrate was precipitated from a solution of calcium nitrate and phosphoric acid by neutralization with 4 moles of ammonia per mole of P_2O_5. This dihydrate was converted into more basic phosphates if it was retained in contact with the solution and the pH was raised above 4 by further addition of ammonia. The rate of conversion was increased by an increase of temperature and the presence of fluoride ions in solution. When there were fluoride ions in solution the final product was always pentacalcium fluoride trisphosphate and the conversion rate was increased by the absence of Ca^{2+} ions in solution. When fluoride ions were absent, the final product varied from tetracalcium hydrogen trisphosphate through tricalcium bisphosphate hydrate to pentacalcium hydroxide trisphosphate, according to the other experimental conditions. The various water-insoluble calcium phosphates obtained were identified by *X*-ray powder diffraction and quantitative chemical analysis.

TABLE 1 below lists the names and formulæ of the water-insoluble calcium phosphates in order of increasing basicity. The abbreviations given will be used in Tables in the Experimental section.

TABLE 1.

Compound	Formula	Molar ratio, $CaO : P_2O_5$	Abbreviation
Calcium hydrogen phosphate dihydrate	$CaHPO_4,2H_2O$	2	CHPh
Calcium hydrogen phosphate	$CaHPO_4$	2	CHP
Tetracalcium hydrogen trisphosphate trihydrate	$Ca_4H(PO_4)_3,3H_2O$	$2\frac{2}{3}$	4CHPh
Tricalcium bisphosphate hydrate	$Ca_3(PO_4)_2,xH_2O$	3	3CPh
Pentacalcium hydroxide trisphosphate	$Ca_5(OH)(PO_4)_3$	$3\frac{1}{2}$	5C(OH)P
Pentacalcium fluoride trisphosphate	$Ca_5F(PO_4)_3$	$3\frac{1}{2}$	5CFP

The most basic calcium phosphate [$Ca_5X(PO_4)_3$; X = F or OH] is a definite crystalline compound of known structure (cf. *e.g.*, refs. 1—3), but the distinct existence of the slightly less basic compounds $Ca_4H(PO_4)_3,3H_2O$ and $Ca_3(PO_4)_2,xH_2O$ has often been queried, mere calcium deficiency in the " apatite " structure being proposed. However, although complete structural analyses for these two materials have not yet been made their lattice

[1] St. Naray-Szabo, *Z. Krist.*, 1930, **75**, 387.
[2] Mehmel, *Z. Krist.*, 1930, **75**, 323.
[3] Posner, Perloff, and Diorio, *Acta Cryst.*, 1958, **11**, 308.

types are known: that of $Ca_4H(PO_4)_3,3H_2O$ differs from that of apatite;[4] that of $Ca_3(PO_4)_2,xH_2O$ is isomorphous with apatite but discrete.[5] Moreover, our own studies confirm that the basicity of the calcium phosphates changes in discrete steps, and not smoothly once calcium hydrogen phosphate is passed.

The precipitation and stability of (water-insoluble) calcium hydrogen phosphate (dihydrate and anhydrous) from various water-soluble phosphates have been studied by several workers [6-9] as they are of considerable technical importance in the manufacture of some fertilizers. Results have, in general, been contradictory and conflicting, owing frequently to poor understanding and characterization of the reaction products. It can be seen from Table 1 that there are six possible water-insoluble products which may occur singly, or as several together.

Accordingly, the following experiments were made as an initial study in the precipitation of water-insoluble phosphates to determine the conditions under which the calcium hydrogen phosphates are precipitated and under which they are converted into the more basic calcium phosphates. In addition, the presence in the solution of fluoride ions was examined to find how they affected the production of the apatite phase, since in certain phosphate processes the formation of pentacalcium fluoride trisphosphate is undesirable as it represents a return to the original phosphate source.

The composition of precipitates was obtained by *X*-ray powder diffraction analysis, supplemented where necessary by chemical analysis of the products.

Experimental

A solution of calcium nitrate and phosphoric acid containing 1·11 moles of P_2O_5 per l. and having a $CaO : P_2O_5$ molar ratio of 3·4 was prepared. 10·0 ml. portions of this solution were added severally to 200, 1000, 2500, and 5000 ml. of water. The pH was measured, by using glass and calomel electrodes, as 5% ammonia solution was added in 1 ml. portions.

When the first equivalence point at pH 4·5 had been passed, a permanent precipitate appeared and the pH fell below 4·5. On the addition of further ammonia the pH increased, but it fell again after a minute's stirring to a value which remained steady. This effect continued until the second equivalence point was reached. After the second equivalence point had been passed the precipitate was filtered off and submitted to *X*-ray analysis (see Appendix).

Fig. 1 shows the pH–titration curves obtained, and Table 2 gives the composition of the precipitate obtained in this experiment.

Several experiments were carried out in which 300 ml. portions of the solution containing 1·11 moles of P_2O_5 per l. were neutralized with gaseous ammonia in a beaker equipped with a baffle and a powerful stirrer (agitation at 1000 r. p.m.). At intervals during the neutralization two samples were simultaneously withdrawn from the beaker; these were filtered, and the

Table 2.

Titration of solutions containing $Ca(NO_3)_2$ and H_3PO_4 with NH_3 to second equivalence point.

Titrn. no.	Initial soln. (mole of P_2O_5 per l.)	*X*-Ray analysis of precipitate
1	0·0022	CHPh absent, 20% of 5C(OH)P, remainder 4CHPh or 3CPh
2	0·0045	As above, but with 65—70% of 5C(OH)P
3	0·0112	As above, but with 80% of 5C(OH)P
4	0·0558	Precipitate completely CHPh

solids were washed with the minimum quantity of water. One solid was then washed with acetone, air-dried, and analysed by *X*-ray diffraction.

The filtrate from the other sample was analysed for P_2O_5 and NH_3, and the pH of the

[4] Brown, Lehr, Smith, and Frazier, *J. Amer. Chem. Soc.*, 1957, **79**, 5318.
[5] Wallaeys and Montel, *Bull. Soc. chim. France*, 1959, 496.
[6] Montel, *Bull. Soc. chim. France*, 1953, 506.
[7] Brosheer and Lenfesty, *J. Agr. Food Chem.*, 1958, **6**, 827.
[8] Bassett, jun., *Z. anorg. Chem.*, 1907, **53**, 34, 49; 1908, **59**, 1.
[9] Kurmies, *Phosphorsaure*, 1953, **13**, 57.

solution was measured. Ammonia was determined by distillation into standard acid. The solid phase was dissolved in acid and the P_2O_5 content obtained by the vanadomolybdate colour method.

A " neutralization curve " was obtained from the results by plotting the reduction in

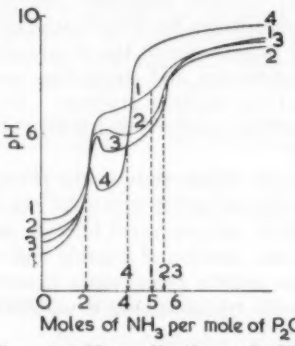


FIG. 1. Neutralization of dilute solutions of H_3PO_4 and $Ca(NO_3)_2$ with NH_3. P_2O_5 contents: (1) 0·0022, (2) 0·0045, (3) 0·0112, and (4) 0·0558 mole $l.^{-1}$.

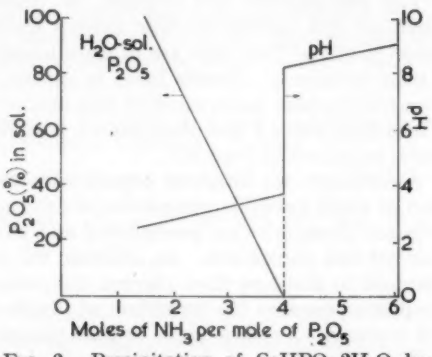


FIG. 2. Precipitation of $CaHPO_4,2H_2O$ by addition of NH_3. Rate of addition 0·01, 0·03, 0·05, or 0·06 mole/min. Temp., 26°, 70°, or 90°.

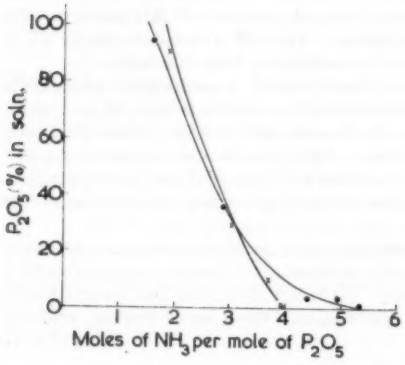


FIG. 3. Influence of fluoride ion on the precipitation of $CaHPO_4,2H_2O$ (cf. Fig. 2). Molar ratio $CaO : P_2O_5$ 3·4 and $F : P_2O_5$ 0·83. P_2O_5 content 1·11 moles $l.^{-1}$. × At 26°; ● at 70°.

P_2O_5 content of the solution against the moles of ammonia added per mole of P_2O_5; pH change was also plotted. The neutralizations were made at rates of 0·01, 0·03, 0·05, and 0·06 mole of NH_3 per min. and initial temperatures of 26°, 70°, and 90°. The curves obtained were all similar and are therefore given combined in Fig. 2.

If the precipitated $CaHPO_4,2H_2O$ was left overnight in the beaker before being submitted for *X*-ray analysis it was found to have been partially, or in some cases largely, converted into an apatite. Further experiments were therefore carried out by starting with precipitated $CaHPO_4,2H_2O$.

The salt $CaHPO_4,2H_2O$ (2 moles $l.^{-1}$) was added to a solution containing ammonium nitrate (4 moles $l.^{-1}$) and calcium nitrate (1·5 moles $l.^{-1}$), and the suspension was agitated. This system simulates the conditions existing at the completion of precipitation of $CaHPO_4,2H_2O$ from a $Ca(NO_3)_2$–H_3PO_4 solution containing an excess of calcium. The pH of the suspension was maintained at 8 by the addition of ammonia and samples were removed at intervals and analysed by *X*-ray diffraction after the usual washing and drying.

This experiment was carried out at 20° and 50°. The results are given in Table 3, which shows the relative amounts of $Ca_3(PO_4)_2,xH_2O$ and $Ca_5OH(PO_4)_3$, obtained.

TABLE 3.

The rate of conversion of $CaHPO_4,2H_2O$ into $Ca_5OH(PO_4)_3$ at pH 8; calcium ions present in solution.

At 20°				At 50°			
Time (hr.)	CHPh (%)	3CPh (%)	5C(OH)P (%)	Time (hr.)	CHPh (%)	3CPh (%)	5C(OH)P (%)
1	100	—	—	½	100	—	—
2	100	—	—	1	100	—	—
3	100	—	—	1½	80	← 20 →	
6	95	← 5 →		2	60—70	← 30—40 →	
22½	70	← 30 →		3	20	← 80 →	
24	40—45	← 55—60 →		4	5—10	← 90—95 →	
27	2—3	60—70	25—35	5	2—3	65—70	30—35
30	Trace	55—65	35—45	6	Nil	55—60	40—45
48	Nil	25—30	70—75	22½	Nil	10—15	85—90

The above two experiments were repeated but this time the solution phase did not contain calcium. The resulting rate of disappearance of $CaHPO_4,2H_2O$ is shown in Table 4.

TABLE 4.

The rate of conversion of $CaHPO_4,2H_2O$ into $Ca_4H(PO_4)_3,3H_2O$ at pH 8; calcium ions absent from solution at 50°.

Time (hr.)	½	1½	2¾	4	6
X-Ray analysis:					
CHPh (%)	98	60—65	15	0	0
4CHPh (%)	2—3	35—40	85	100	100

At 20°, change was very slow. After 30 hr., only 5% of 4CHPh was detected.

Experiments were carried out in which fluoride was added as potassium fluoride to the solution containing 1·11 moles of P_2O_5 per l., which was then neutralized as described above. Two neutralizations were carried out, at 20° and 70°, samples being taken at intervals for chemical and *X*-ray analyses. At 20° the "neutralization curve" and the *X*-ray analysis of precipitates showed apatite formation had not taken place up to the point of complete precipitation of $CaHPO_4,2H_2O$. At 70°, however, $Ca_5F(PO_4)_3$ was being formed in the final stages of precipitation. Fig. 3 shows the precipitation curves at 26° and 70°, for comparison with Fig. 2 where no fluoride was present. Analyses of the precipitates are given in Table 5.

From the *X*-ray and chemical analyses it was concluded that the apatite produced was completely $Ca_5F(PO_4)_3$, with no $Ca_5OH(PO_4)_3$ at any stage of the neutralization. The calcium was determined by EDTA titration, and fluorine by the method of Willard and Winter.[10]

The experiments starting with precipitated $CaHPO_4,2H_2O$ were repeated, this time with fluorine added to the solution phase. With calcium present in the solution phase, the rates of formation of $Ca_5F(PO_4)_3$ were obtained at 20° and 50°; the results are given in Table 6.

TABLE 5.

Neutralization at 70° with gaseous NH_3. Solution concentration 1·11 moles P_2O_5 per l.; mole ratios 3·4 for $CaO : P_2O_5$, 0·83 for $F : P_2O_5$.

Sample no.	Moles of NH_3 added per mole of P_2O_5	pH of H_2O-sol. part	*X*-Ray analysis of ppt.	Mole ratio: $F : P_2O_5$	Mole ratio: $CaO : P_2O_5$
1	1·3	2·3	—	—	—
2	2·9	2·7	—	—	—
3	4·4	3·95	CHP only	—	—
4	4·95	4·6	85—90% of 5CFP	0·63	3·2
5	5·31	6·6	95% of 5CFP	0·65	3·3
6	—	7·9	All 5CFP	0·64	3·2
7	6·09	8·4	All 5CFP	—	—

When calcium was absent from the solution, the rate of conversion of $CaHPO_4,2H_2O$ was greatly increased, as is shown in Table 7.

[10] Willard and Winter, *Ind. Eng. Chem. Anal.*, 1933, **5**, 7.

TABLE 6.

Rate of formation of $Ca_5F(PO_4)_3$. Solution pH 8. (Solution contains $Ca(NO_3)_2$ 1·5 moles, NH_4NO_3 4 moles, KF 0·25 mole, and $CaHPO_4,2H_2O$ 2 moles.)

At 20°					At 50°				
	X-Ray analysis of ppt.					*X*-Ray analysis of ppt.			
Time (hr.)	CHPh (%)	CHP (%)	5CFP (%)	CaF_2 (%)	Time (hr.)	CHPh (%)	CHP (%)	5CFP (%)	CaF_2 (%)
½	98	0	2	s.t.	20/60	100	0	t	s.t.
1	↓	0	↓	t	35/60	85—90	0	10—15	s.t.
1½	↓	0	↓	t	50/60	35—40	20	40—45	s.t.
2	96	0	4	t	1¼	5	5	90	t
3	5—10	0	90—95	0	2	2—3	0	97	t
4	5	0	95	0	3	0	0	100	t
5	3	0	97	0	6	0	0	100	t
6	0	0	100	0					
7	0	0	100	0					

t = trace. s.t. = slight trace.

TABLE 7.

Solution pH 8. Solution contains 4 moles of NH_4NO_3 and 0·025 mole of KF, at 20°.

	X-Ray analysis				*X*-Ray analysis		
Time (hr.)	CHPh (%)	5CFP (%)	CaF_2 (%)	Time (hr.)	CHPh (%)	5CFP (%)	CaF_2 (%)
1	98	2	0	4	0	100	Trace
2	60	40	0	5	0	100	Trace
3	10	90	0				

At 50° instantaneous conversion into $Ca_5F(PO_4)_3$ occurred.

To find the effect on the conversion of $CaHPO_4,2H_2O$ into $Ca_5F(PO_4)_3$ at lower pH when calcium is absent from the solution phase, solid $CaHPO_4,2H_2O$ was stirred in a solution of ammonium nitrate containing potassium fluoride at 50°. The pH of the solution had not been raised by addition of ammonia and was initially 6·5, falling to 5 as conversion proceeded. Even under these conditions formation of $Ca_5F(PO_4)_3$ was rapid, being almost complete within 10 min.

DISCUSSION

Table 8 summarises diagrammatically the results of the experiments discribed in the experimental section, showing the products existing under various conditions at different times.

As a solution of calcium nitrate and phosphoric acid is neutralized with ammonia solution, the pH–ammonia-addition curve shows a first equivalence point at 2 moles of NH_3 per mole of P_2O_5 and pH 4 (all curves Fig. 1), corresponding to the formation of calcium tetrahydrogen bisphosphate in solution:

$$Ca(NO_3)_2 + 2H_3PO_4 + 2NH_3 \longrightarrow Ca(H_2PO_4)_2 + 2NH_4NO_3$$

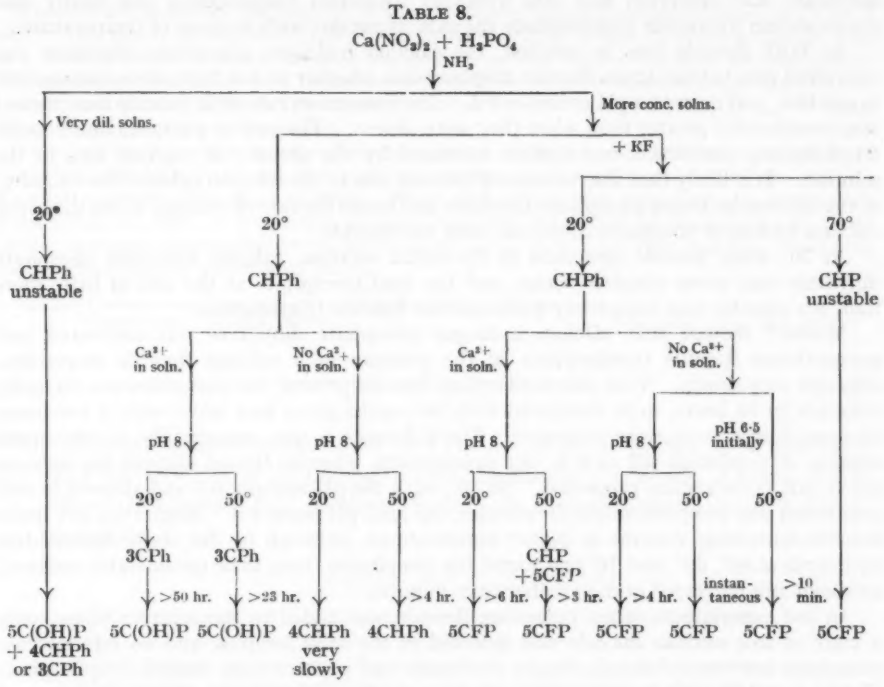
Curve 4 of Fig. 1 for the most concentrated solution in this first experiment shows a second equivalence point at 4 moles of NH_3 per mole of P_2O_5 and pH 6, corresponding to the formation of insoluble calcium hydrogen phosphate dihydrate:

$$Ca(NO_3)_2 + H_3PO_4 + 2NH_3 \longrightarrow CaHPO_4 + 2NH_4NO_3$$

That the precipitate obtained was indeed calcium hydrogen phosphate was confirmed by *X*-ray analysis.

Curves 1, 2, and 3 are for the more dilute solutions, and all three had their second equivalence points at 5 or more moles of NH_3 per mole of P_2O_5 and pH 6·5—8, indicating that calcium phosphates more basic than calcium hydrogen phosphate were formed.

TABLE 8.



Tetracalcium hydrogen trisphosphate requires $5\frac{1}{3}$ moles of NH_3 per mole of P_2O_5 for complete production:

$$4Ca(NO_3)_2 + 3H_3PO_4 + 8NH_3 \longrightarrow Ca_4H(PO_4)_3 + 8NH_4NO_3$$

Tricalcium bisphosphate requires 6 moles of NH_3 per mole of P_2O_5:

$$3Ca(NO_3)_2 + 2H_3PO_4 + 6NH_3 \longrightarrow Ca_3(PO_4)_2 + 6NH_4NO_3$$

Pentacalcium hydroxide trisphosphate requires $6\frac{2}{3}$ moles of NH_3 per mole of P_2O_5:

$$5Ca(NO_3)_2 + 3H_3PO_4 + 10NH_3 + H_2O \longrightarrow Ca_5(PO_4)_3(OH) + 10NH_4NO_3$$

X-Ray analysis showed the precipitates in these three cases to be mixtures of the more basic phosphates.

From solutions more concentrated than these first four, only calcium hydrogen phosphate dihydrate was precipitated and it could be filtered off, except in the case of a solution containing fluoride ions at 70°. Fig. 2 shows the P_2O_5 solubility curve reaching zero at the theoretical molar $NH_3 : P_2O_5$ ratio of 4. The same line was obtained over the wide range of neutralization rates and temperatures given in the Experimental section. When the calcium hydrogen phosphate dihydrate was retained in contact with the solution existing at the end of precipitation (maintained at pH 8) it was converted into a more basic calcium phosphate, the exact phosphate depending on the solution contents:

(*a*) With no fluoride or calcium ions in solution the calcium hydrogen phosphate dihydrate went to the next more basic phosphate, tetracalcium hydrogen trisphosphate, the rate increasing with increase of temperature.

(*b*) With no fluoride but with calcium ions in solution the calcium hydrogen phosphate

dihydrate was converted first into hydrated tricalcium bisphosphate and finally into pentacalcium hydroxide trisphosphate the rate increasing with increase of temperature.

(*c*) With fluoride ions in solution, the calcium hydrogen phosphate dihydrate was converted into pentacalcium fluoride trisphosphate whether or not there were calcium ions in solution, and even at a pH as low as 6·5. The conversion rate with fluoride ions present was considerably greater than when they were absent. The rate of pentacalcium fluoride trisphosphate production was further increased by the absence of calcium ions in the solution. It is likely that the presence of calcium ions in the solution reduces the solubility of the calcium hydrogen phosphate dihydrate and hence the rate of reaction of the dissolved calcium hydrogen phosphate dihydrate with the fluoride.

At 70° when fluoride ions were in the initial solution, calcium hydrogen phosphate dihydrate was never obtained alone, and the final precipitate at the end of little more than ten minutes was completely pentacalcium fluoride trisphosphate.

Montel [6] showed that calcium hydrogen phosphate dihydrate was converted into pentacalcium fluoride trisphosphate in the presence of a calcium fluoride suspension, although very slowly. With dissolved sodium fluoride present, the conversion was virtually complete in 24 hours, to be compared with the results given here where only a few hours at room temperature were necessary. The difference is due, presumably, to the maintenance of a solution pH of 8 in our experiments, whereas Montel allowed his solution pH to fall as conversion proceeded. At 50°, with the pH initially 6·5 and allowed to fall, conversion was complete within 10 minutes, the final pH being 4·8. Montel did not study fluoride-containing systems at higher temperatures, although he did study fluoride-free hydrolysis at 40°, 50°, and 70° and found the completion times to be considerably reduced, although still measured in days rather than minutes.

In our experiments, when potassium fluoride was added to the solution phase, only a trace of free calcium fluoride was detected in the solid samples, and no intermediate phosphate between calcium hydrogen phosphate and pentacalcium fluoride trisphosphate (Tables 5 and 6). Kurmies [9] suggests that pentacalcium fluoride trisphosphate is formed from calcium hydrogen phosphate *via* pentacalcium hydroxide trisphosphate, a view which our results would not support. Scharrer, Gericke, and Jung [11] consider the hydroxyl ions in pentacalcium hydroxide trisphosphate are too strongly bound to exchange with fluoride ions, whereas Montel [12] and McCann [13] claim to have obtained such an exchange.

Conclusions.—It is possible to precipitate calcium hydrogen phosphate dihydrate completely from all but very dilute (0·005 g. of P_2O_5 per l.) solutions of calcium nitrate and phosphoric acid neutralized by 4 moles of NH_3 per mole of P_2O_5 over a wide range of temperatures and rates. The precipitate is stable if filtered off at once, but is converted into more basic calcium phosphates if retained in the solution. The rate of conversion increases with increase of temperature, and if fluoride ions are in the solution. At 70° with fluoride ions in solution, calcium hydrogen phosphate cannot be obtained alone.

The chemical analyses were carried out by Miss M. O. Oxborrow and Mr. V. C. Vinyard.

Appendix: X-*Ray Powder Diffraction Analysis.*—Calcium hydrogen phosphate and calcium tetrahydrogen bisphosphate (both anhydrous and hydrated) give sharp *X*-ray powder-diffraction patterns; there is, thus, no difficulty or ambiguity in determining their occurrence. Laboratory preparations of hydrated tricalcium bisphosphate, tetracalcium hydrogen triphosphate trihydrate, pentacalcium hydroxide trisphosphate, and pentacalcium fluoride trisphosphate give similar, very blurred patterns, corresponding to that of mineral apatite. It is, therefore, very difficult to decide from a laboratory-prepared sample which of these materials is present, or if a mixture of them exists. A distinction is, however, possible if the sample is heated to about 850° for a few hours, and then the *X*-ray pattern again measured.

[11] Scharrer, Gericke, and Jung, *Z. Pflanzenernährung, Düng.*, 1953, **60**, 250.
[12] Montel, *Compt. rend.*, 1956, **242**, 1182.
[13] McCann, *J. Biol. Chem.*, 1953, **201**, 247.

Apatites are stable (in the absence of any chemically reacting components) up to at least 1450°. The effects of the heating are to improve crystallinity and increase crystallite size, both of which produce a much sharper *X*-ray powder pattern, similar to that of mineral apatite. Distinctions between fluoro- and hydroxy-compounds are based on fine details of this pattern.

Hydrated tricalcium bisphosphate is dehydrated at ~700° to give β-$Ca_2(PO_4)_2$, of sharp distinguishable *X*-ray powder pattern.

Tetracalcium hydrogen trisphosphate trihydrate decomposes at 850° to a mixture of β-$Ca_2(PO_4)_2$ and β-$Ca_2P_2O_7$; the *X*-ray powder pattern of a heated sample, therefore, consists of a mixture of these two sharp patterns. Since calcium hydrogen phosphate also decomposes to β-$Ca_2P_2O_7$ at 850°, a distinction between hydrated tricalcium bisphosphate and tetracalcium hydrogen trisphosphate trihydrate can be made only if calcium hydrogen phosphate is largely absent from the original sample.

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LEVINGTON, IPSWICH, SUFFOLK.

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968. *Aromatic Reactivity: Part XVIII.*[1] *Acid Cleavage of Trimethylsilyl Derivatives of Diphenyl Ether, Diphenyl Sulphide, Furan, Thiophen, Benzothiophen, Dibenzofuran, Dibenzothiophen, and 9-Ethylcarbazole.*

By C. EABORN and J. A. SPERRY.

We have prepared the 2- and 4-trimethylsilyl derivatives of diphenyl ether and diphenyl sulphide, the 2-derivatives of furan and thiophen, the 2- and 3-derivatives of benzothiophen, the 1-, 2-, 3-, and 4-derivatives of dibenzofuran and dibenzothiophen, and the 3-derivative of 9-ethylcarbazole, and have measured their rates of cleavage at 50° by a mixture of methanol (5 vol.) and aqueous perchloric acid (2 vol.). The results are analysed and, where possible, compared with those for common electrophilic substitutions in the parent aromatic compounds.

WE have prepared some mono-trimethylsilyl derivatives of diphenyl ether, diphenyl sulphide, furan, thiophen, benzothiophen, dibenzofuran, dibenzothiophen, and 9-ethylcarbazole, and have measured spectrophotometrically their rates of cleavage at 50° by mixtures of methanol (5 vol.) and aqueous perchloric acid (2 vol.). The results are shown in the Table as observed first-order rate constants, k, at the (added-)acid concentrations listed, along with rates, k_{rel}, relative to that of phenyltrimethylsilane. The wavelengths, λ, used to study the cleavage are also listed. Not all the compounds were examined at the same acid concentration, and some values of k_{rel} are derived by the "overlap" procedure used before.[2,3]

The value of k_{rel} for the compound x-Me_3Si·Ar is referred to below, loosely but conveniently, as the reactivity of the x-position of the aromatic compound ArH in protodesilylation; this facilitates comparison of the results with those for simple electrophilic substitutions, such as halogenation, nitration, and detritiation. In the diagrams below, the reactivities are shown at the appropriate positions of the aromatic systems.

The features of the results are as follows:

(i) The 2- and the 4-position of diphenyl ether are distinctly less reactive in protodesilylation than the corresponding positions of anisole (for which k_{rel} is 1510 for the 4- and 355 for the 2-position [2]). The difference is relatively greater for the 2- than for the 4-position.

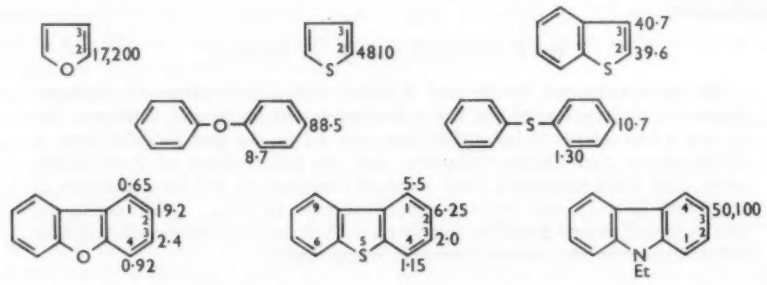
[1] Part XVII, Eaborn and Pande, *J.*, 1961, 3715.
[2] Eaborn, *J.*, 1956, 4858.
[3] Deans and Eaborn, *J.*, 1959, 2299.

The 2- and the 4-position of diphenyl sulphide are much less reactive than the corresponding positions of diphenyl ether, as would be expected from the smaller $+T$ effect of a sulphur atom than of an oxygen atom.

(ii) The 2-position of furan is several times more reactive than the 2-position of thiophen. It seems to be accepted that this is generally the case in electrophilic substitution, but, as far as we are aware, the present results represent the first measurement of the relative reactivities. The lower reactivity of thiophen is another consequence of the smaller $+T$ effect of a sulphur than of an oxygen atom.

(iii) Fusion of a benzene ring with a thiophen ring, to give benzothiophen, results in a large decrease in reactivity at the 2-position of the thiophen ring and a comparatively small decrease at the 3-position. The large change at the 2-position can be associated with the fact that the $+T$ effect of the sulphur atom can only reach this position in benzothiophen by disturbing the conjugation within the benzene ring, as shown in structure (I) for the Wheland intermediate.[4,5] This is not so for the 3-position [see structure (II)], and the small lowering of reactivity at this position can be attributed to a drawing-off of part of the $+M$ effect of the sulphur atom from the thiophen ring into the benzene ring [cf. process (III)].

It is noteworthy that the reactivities of the 2- and the 3-position of benzothiophen are nearly equal in protodesilylation. In detritiation, the 3-position is clearly the more reactive, but it is less than 1·5 times as reactive as the 2-position.[6] On nitration only the



3-nitro-product has been isolated,[7] but a recent preliminary communication indicates, more acceptably, that at least 10—15% of 2-substitution also occurs.[8] Friedel–Crafts acylation gives up to 33% of 2- along with predominant 3-substitution,[9] but molecular bromination,[10] chloromethylation,[11] and mercuration [12] seem to result in 3-substitution only.

(iv) Closure of the five-membered ring on going from diphenyl ether or diphenyl sulphide to dibenzofuran or dibenzothiophen is associated with a lowering of reactivity at positions *ortho* and *para* to the heteroatom, as has been noted for the oxygen compounds in nitration.[13] In part this may be because the 4- and the 2-position of the dibenzo-compounds, while *ortho* and *para*, respectively, to the heteroatoms, are also *meta* to a substituted phenyl

[4] Hartough and Meisel, "Heterocyclic Compounds. Compounds with Condensed Thiophene Rings," Interscience Publ. Inc., New York, 1954, p. 5.
[5] Katritzky and Lagowsky, "Heterocyclic Chemistry," Methuen and Co., Ltd., London, 1960, p. 162.
[6] Eaborn and Baker, unpublished results.
[7] Fries and Hemmecke, *Annalen*, 1929, **470**, 1; ref. 4, p. 48.
[8] van Zyl, van Dyke, Heasley, de Jongh, Bredeweg, and Neckers, 4th Report on Research under Sponsorship of Petroleum Research Fund, Amer. Chemical Soc., Washington, 1960, p. 39.
[9] Farrar and Levine, *J. Amer. Chem. Soc.*, 1950, **72**, 4433.
[10] Komppa, *J. prakt. Chem.*, 1929, **122**, 319; Crook and Davies, *J.*, 1937, 1697; Szmuszkovicz and Modest, *J. Amer. Chem. Soc.*, 1950, **72**, 571.
[11] Blicke and Sheets, *J. Amer. Chem. Soc.*, 1948, **70**, 3768.
[12] Challenger and Miller, *J.*, 1939, 1005.
[13] Dewar and Urch, *J.*, 1957, 345; 1958, 3079.

Cleavage of $ArSiMe_3$ compounds at 25°.

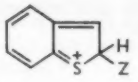
Parent compd. ArH	Posn. of Me_3Si	λ (mμ)	$[HClO_4]$ [a] (M)	10^3k (min.$^{-1}$)	k_{rel}
Benzene	1	270	9·45	1·92	1
	1	270	12·07	7·86	1
Toluene	4	273	9·45	38·3	20·0
	4	273	7·66	14·7	—
Ph_2O	2	285	12·07	68·7	8·73
	4	250	6·05	27·5	—
	4 [b]	250	7·66	65·0	88·5
	4 [b]	250	7·66	65·0	88·5
Ph_2S	2	304	12·07	10·2	1·30
	4	303	9·45	20·5	10·7
Furan	2	231	0·56	42·2	17,200
Thiophen	2	255	0·56	11·8	(4810) [c]
Benzothiophen	2	306	9·45	76·1	39·6
	2	306	6·05	12·5	—
	3	306	9·45	78·1	40·7
Dibenzofuran	1	254	12·07	5·12	0·65
	2	224	9·45	36·9	19·2
	3	255	9·45	4·58	2·39
	3	255	12·07	18·9	2·41
	4	236	12·07	7·26	0·92
Dibenzothiophen	1	291	12·07	43·6	5·53
	2	286	9·45	12·0	6·25
	3	290	12·07	15·7	2·00
	4	291	12·07	9·03	1·15
$2,4,6\text{-}C_6H_3Me_3$	1	277	0·20	40·3	53,000 [d]
9-Ethylcarbazole	2	270	0·20	38·1	50,100

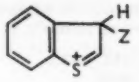
[a] Concn. of aqueous acid, 2 ml. of which were added to 5 ml. of a methanolic solution of the organosilane. [b] One sample was made by the Wurtz–Fittig reaction and the other by use of a Grignard reagent. [c] Unpublished result by Miss P. M. Greasley. [d] Value from ref. 2.

group, which, like the phenyl group itself,[14] probably deactivates *meta*-positions. Mainly, however, it can be attributed to the fact that in the closed-ring compounds the lone-pairs of electrons of oxygen and sulphur are largely engaged in the resonance which gives aromatic character to the five-membered ring, and the $+T$ effects of these atoms can reach the exposed positions of the benzene rings only at the expense of this aromatic character.

It is not clear why the reduction in reactivity should be greater for the oxygen than for the sulphur compounds. The relatively large reduction of reactivity *ortho* to the heteroatom in the case of the oxygen compounds, and the very small corresponding reduction in the case of the sulphur compounds, result in the 4-position of dibenzofuran's being less reactive than that of dibenzothiophen, although the 2-position of diphenyl ether is several times more reactive than that of diphenyl sulphide. The 2-position of dibenzofuran, however, is several times more reactive than that of dibenzothiophen.

Almost certainly the 3-positions of diphenyl ether and diphenyl sulphide are deactivated in protodesilylation (compare the deactivation by a *m*-OMe group [3]), but the corresponding


(I)


(II)

(III)

positions, the 3-positions, in the dibenzo-compounds are clearly activated. This activation can be associated with the phenyl group *para* to the 3-position, electron-release from this group being facilitated by the coplanarity of the two benzene rings (cf. ref. 15).

[14] Eaborn and Taylor, *J.*, 1961, 1012.
[15] de la Mare and Ridd, "Aromatic Substitution. Nitration and Halogenation," Butterworths Scientific Publ., London, 1959, p. 158.

Halogenation [16,17] and sulphonation [18,19] of dibenzo-furan and -thiophen seem to take place exclusively at the 2-position,* and, since these are reactions of higher selectivity, this is consistent with the protodesilylation results (the reactivity of the 1-position of dibenzothiophen in this reaction being neglected for reasons given below). Nitration of dibenzothiophen, while complicated by oxidation at the sulphur atom, seems to occur wholly or mainly at the 2-position,[16,20] but nitration of dibenzofuran is reported to give, in acetic acid, predominant 3-substitution (up to 80%,[22] we ourselves obtaining 75% of the 3-nitro-compound), or, in acetic anhydride, equal amounts of 2- and 3- along with considerable 1-substitution.[13] It has been suggested that the 3-orientation in dibenzofuran arises from prior protonation of the oxygen atom, which would cause preferential deactivation of 2- and 4-positions,[23] but this would result in overall deactivation of all positions, whereas the partial rate factor for both the 2- and the 3-position in nitration in acetic anhydride is 94. The nitration result is at present inexplicable,† as is the exclusive 4-substitution reported in mercuration.[25]

(v) There is a fairly large difference between the measured reactivity of the 1-position in dibenzofuran and in dibenzothiophen, the former being somewhat deactivated and the latter activated several-fold. At first sight the reactivity of the 1-position of dibenzothiophen might appear much too high, since 1-substitution is not reported in the common electrophilic substitutions. However, protodesilylation is known to be liable to steric acceleration by *ortho*-substituents,[26,27] and the high reactivity of the 2-position of biphenyl in this reaction ($k_{rel} = 6{\cdot}0$) compared with that of the 4-position ($k_{rel} = 2{\cdot}8$) ‡ has been attributed to interference between the 2′-H atom and the 2-Me_3Si group.[27] The relative reactivities of the 1- and the 3-position of dibenzothiophen are in good agreement with the results in biphenyl if it assumed that similar interference occurs between the 1-Me_3Si group and the 9-H atom, and that the sulphur atom affects the 1- and the 3-position which are both *meta* to it, to about the same extent.

It thus seems that it is the low reactivity of the 1-position of dibenzofuran which is anomalous; similar steric acceleration would be expected, and it is difficult to believe that a six-fold deactivation by polar effects exists to compensate for it.

(vi) In the study of 9-ethyl-3-trimethylsilylcarbazole, it was first shown spectrophotometrically that 9-ethylcarbazole was not protonated to a detectable extent even in media much stronger in acid than that used for cleavage, and it can be safety assumed that the trimethylsilyl derivative was also present wholly as free base.

The reactivity of the 3-position (the most reactive position) of 9-ethylcarbazole in protodesilylation is very much greater than that of the corresponding 2-position in dibenzofuran or -thiophen, and accords with the much greater reactivity of the compound

* The facts are that only the 2-substituted compound was isolated pure in each case. The possibility of formation of other isomers is not excluded by the experimental results. Acetylation of dibenzothiophen almost certainly gives other isomers, but only the 2-acetyl derivative has been isolated in appreciable quantity, along with small amounts of the 4-isomer.[20, 21]

† In a recent theoretical paper, however, the nitration results are considered to be typical and all the other anomalous.[24]

‡ These rate factors refer to measurements in sulphuric acid–acetic acid mixtures,[27] and slightly larger values would be expected in aqueous-methanolic perchloric acid.[3]

[16] Cullinane, Davies, and Davies, *J.*, 1936, 1435.
[17] Mayer and Krieger, *Ber.*, 1922, **55**, 1659.
[18] Gilman, Smith, and Oatfield, *J. Amer. Chem. Soc.*, 1934, **56**, 1412.
[19] Courtot, *Compt. rend.*, 1934, **198**, 2260.
[20] Gilman and Nobis, *J. Amer. Chem. Soc.*, 1949, **71**, 274.
[21] Burger, Wartman, and Lutz, *J. Amer. Chem. Soc.*, 1938, **60**, 2628.
[22] Cullinane, *J.*, 1930, 2267; Gilman, Bywater, and Parker, *J. Amer. Chem. Soc.*, 1935, **57**, 885.
[23] Ref. 4, p. 12.
[24] Brown and Coller, *Austral. J. Chem.*, 1959, **12**, 152.
[25] Gilman and Young, *J. Amer. Chem. Soc.*, 1934, **56**, 1415.
[26] Benkeser and Krysiak, *J. Amer. Chem. Soc.*, 1954, **76**, 6353; Benkeser, Hickner, Hoke, and Thomas, *ibid.*, 1958, **80**, 5289; Eaborn and Moore, *J.*, 1959, 3640; Eaborn, Lasocki, and Webster, *J.*, 1959, 3034.
[27] Deans, Eaborn, and Webster, *J.*, 1959, 3031.

p-$Me_2N{\cdot}C_6H_4{\cdot}SiMe_3$ ($k_{rel} = 3 \times 10^7$) than of the compound *p*-$MeO{\cdot}C_6H_4{\cdot}SiMe_3$ ($k_{rel} = 1510$). Since the spread of rates is normally much greater in nitration than in protodesilylation it is surprising that the partial rate factor for the 3-position of carbazole in nitration, *viz.*, 79,000, is not much greater than the value of k_{rel} in protodesilylation (*viz.*, 50,100), the 9-ethyl group being unlikely to have a large effect. If the nitration results are correct, they seem to indicate that polarizability effects are less important relative to polarization effects in the carbazole system than in dibenzo-furan and -thiophen.

Experimental

General.—Ethylene dibromide was used in the entrainment method of making Grignard reagents,[28] and was added during at least 12 hr. to the refluxing mixture of aryl halide, magnesium, and ether.

Coupling of the Grignard reagent with chlorotrimethylsilane was normally followed by treatment of the reaction mixture with saturated ammonium chloride solution, though sometimes a little dilute sulphuric acid had to be added to produce two clear layers. Washing and drying (Na_2SO_4) of the ethereal layer was followed by removal of the solvent through a short fractionating column and fractional distillation of the residue, usually at reduced pressure, through a more efficient column, and by recrystallization where appropriate.

The excess of lithium was removed by filtration from ethereal solutions of organolithium reagents before coupling. Cross-metallation or metallation was carried out with a slight excess of n-butyl-lithium in ether unless otherwise stated. Coupling with chlorotrimethylsilane was followed by addition of 5% aqueous sulphuric acid, and the organic layer was worked up as described above.

Wurtz–Fittig couplings were followed by filtration through kieselguhr and fractionation of the toluene solution.

In all preparations our aim was to obtain pure samples rather than high yields.

x-*Trimethylsilyldiphenyl Ethers.*—2-Lithiodiphenyl ether, prepared [29] from diphenyl ether (70 g., 0·41 mole) in ether (500 ml.), was coupled during 6 hr. under reflux with chlorotrimethylsilane (50 g., 0·46 mole), to give 2-*trimethylsilyldiphenyl ether* (62 g., 62%), b. p. 137—139°/6 mm. n_D^{20} 1·5525 (Found: C, 74·6; H, 7·7. $C_{15}H_{18}OSi$ requires C, 74·4; H, 7·5%).

Boiling 4-chlorodiphenyl ether (56 g., 0·27 mole), chlorotrimethylsilane (32 g., 0·30 mole) and sodium (14 g., 0·6 g.-atom) in toluene (200 ml.) for 2 hr. gave 4-*trimethylsilyldiphenyl ether* (39 g., 59%), b. p. 147—148°/6 mm., n_D^{20} 1·5505 (Found: C, 74·7; H, 7·4%).

An identical product was obtained in 42% yield from coupling of chlorotrimethylsilane with the Grignard reagent prepared from 4-bromodiphenyl ether by the entrainment method.

x-*Trimethylsilyldiphenyl Sulphides.*—Diphenyl sulphide (100 g., 0·54 mole) was metallated in ether (500 ml.). Coupling during 6 hr. under reflux with chlorotrimethylsilane (62 g., 0·58 mole) gave 2-*trimethylsilyldiphenyl sulphide* (32 g., 23%), b. p. 132—136°/2 mm., n_D^{20} 1·5908 (Found: C, 69·9; H, 7·3. $C_{15}H_{18}SSi$ requires C, 69·7; H, 7·0%).

The Grignard reagent prepared by the entrainment method from 4-bromodiphenyl sulphide (38 g., 0·14 mole) in ether (250 ml.) was coupled during 6 hr. under reflux with chlorotrimethylsilane (19·5 g., 0·18 mole), to give 4-*trimethylsilyl sulphide* (22 g., 60%), b. p. 167—168°/3 mm., n_D^{20} 1·5903 (Found: C, 69·9; H, 7·1%). Attempts to make this compound from 4-chlorodiphenyl sulphide, either by Wurtz–Fittig coupling or through the Grignard reagent, led to recovery of unchanged aryl halide.

2-*Trimethylsilylfuran.*—This ether, b. p. 124—125°, n_D^{20} 1·4467, was prepared by Benkeser and Currie's method.[30].

2-*Trimethylsilylthiophen.*—This compound, prepared from 2-thienyl-lithium and chlorotrimethylsilane in ether, had b. p. 165·5°, n_D^{20} 1·4960 (previously misreported [31] as n_D^{20} 1·4996).

x-*Trimethylsilylbenzothiophens.*—A slight excess of n-butyl-lithium in ether was added to a solution of benzothiophen (50 g., 0·37 mole) in tetrahydrofuran (500 ml.) the mixture being kept at −10°. The volume of ether was made up to that of the tetrahydrofuran, and the

[28] Pearson, Cowan, and Beckler, *J. Org. Chem.*, 1959, **24**, 504.
[29] Gilman and Bebb, *J. Amer. Chem. Soc.*, 1939, **61**, 109.
[30] Benkeser and Currie, *J. Amer. Chem. Soc.*, 1948, **70**, 1780.
[31] Deans and Eaborn, *J.*, 1959, 2303.

mixture was stirred for 2 hr. at room temperature.[32] Coupling during 20 hr. at room temperature with chlorotrimethylsilane (42 g., 0·39 mole) gave **2-*trimethylsilylbenzothiophen*** (20 g., 25%), b. p. 123°/7 mm., n_D^{20} 1·5759 (Found: C, 64·3; H, 7·0. $C_{11}H_{14}SSi$ requires C, 64·0; H, 6·8%).

The Grignard reagent prepared by the entrainment method from 3-bromobenzothiophen (81 g., 0·38 mole) in ether (200 ml.) was coupled during 4 hr. under reflux with chlorotrimethylsilane (45 g., 0·41 mole), to give **3-*trimethylsilylbenzothiophen*** (39 g., 48%), b. p. 120—122°/7 mm., n_D^{20} 1·5800 (Found: C, 64·1; H, 6·7%).

A similar experiment involving 3-chlorobenzothiophen gave only unchanged aryl chloride.

x-*Trimethylsilyldibenzofurans*.—1-Bromo- was prepared from 4-amino-dibenzofuran by Gilman and Van Ess's method.[33] Cross-metallation (10 min. at 0°) of the bromide (23 g., 0·093 mole) in ether (200 ml.), followed by coupling during 18 hr. at room temperature with chlorotrimethylsilane (12 g., 0·11 mole), gave **1-*trimethylsilyldibenzofuran*** (8 g., 36%), b. p. 163—164°/7 mm., n_D^{20} 1·6040 (Found: C, 75·4; H, 6·9. $C_{15}H_{16}OSi$ requires C, 75·0; H, 6·7%).

Contrary to an earlier report,[34] when bromine (160 g., 1 mole) was added to a solution of dibenzofuran (84 g., 0·5 mole) in glacial acetic acid (250 ml.) at 0° no reaction was apparent, but hydrogen bromide was evolved when the mixture was warmed. The temperature was maintained at 50° for 4 hr., and the mixture then added to water. Benzene extraction, followed by removal of the benzene and distillation of the residue, gave 2-bromodibenzofuran (100 g., 80%), m. p. 107—108°. This (50 g., 0·21 mole) was cross-metallated (20 min. under reflux) in ether (200 ml.), and coupling (1 hr. under reflux) with chlorotrimethylsilane (27 g., 0·25 mole) then gave material (24 g., 48%) of m. p. 39—41°. Recrystallization from methanol gave **2-*trimethylsilyldibenzofuran***, m. p. 44° (Found: C, 75·2; H, 6·8%).

A product obtained by Wurtz–Fittig coupling from the 2-bromo-compound could not be satisfactorily purified.

3-Nitro- was converted into 3-amino-dibenzofuran,[35] and from this the 3-bromo-compound, m. p. 120—122°, was prepared by the Sandmeyer reaction. The bromide (45 g., 0·16 mole), chlorotrimethylsilane (19·5 g., 0·18 mole) and sodium (8·5 g., 0·37 g.-atom) in boiling toluene (200 ml.) (2 hr.) gave an oil, b. p. 140—148°/3—4 mm., and recrystallization from methanol gave **3-*trimethylsilyldibenzofuran*** (12 g., 27%), m. p. 49° (Found: C, 74·8; H, 6·6%).

Dibenzofuran (35 g., 0·21 mole) was metallated (24 hr. under reflux) in ether (200 ml.). Coupling (4 hr. at room temperature, then 2 hr. under reflux) with chlorotrimethylsilane (26 g., 0·24 mole) gave an oil, b. p. 143—147°/3 mm., which recrystallized from methanol, to give dibenzofuran (10·5 g., 0·063 mole) and **4-*trimethylsilyldibenzofuran*** (12 g., 54% based on unrecovered dibenzofuran), m. p. 41° (Found: C, 74·9; H, 6·9%).

x-*Trimethylsilyldibenzothiophens*.—1-Bromo- was prepared from 2-acetamidodibenzothiophen.[36] The bromide (13 g., 0·049 mole) was cross-metallated (15 min. at 0°) in ether (100 ml.); coupling during 2 hr. under reflux with chlorotrimethylsilane (6·5 g., 0·06 mole) gave **1-*trimethylsilyldibenzothiophen*** (7 g., 51%), b. p. 160—161°/2—3 mm., n_D^{20} 1·6408 (Found: C, 70·4; H, 6·4. $C_{15}H_{16}SSi$ requires C, 70·3; H, 6·3%) (cf. ref. 37).

The 2-isomer, m. p. 49°, was made in 71% yield by Illuminati, Nobis, and Gilman's method,[38] 10 min. being allowed for cross-metallation.

The 3-isomer, m. p. 104—105°, was made in 64% yield by Illuminati, Nobis, and Gilman's method.[38]

The 4-isomer, b. p. 153°/1 mm., n_D^{20} 1·6342, was made in 45% yield by Gilman and Nobis's method,[39] 19 hr. being allowed for metallation.

9-*Ethyl*-3-*trimethylsilylcarbazole*.—3-Bromo-9-ethylcarbazole (40 g., 0·145 mole) in benzene (300 ml.) was stirred for 3 hr. at room temperature with n-butyl-lithium (0·15 mole) in ether (200 ml.). Coupling during 20 hr. at room temperature with chlorotrimethylsilane (21·5 g., 0·2 mole) gave an oil, b. p. 160—170°/1 mm., which crystallised from methanol to give **9-*ethyl*-3-*trimethylsilylcarbazole*** (31 g., 77%) (Found: C, 76·1; H, 8·0. $C_{17}H_{21}NSi$ requires C, 76·35; H, 7·9%).

[32] Shirley and Cameron, *J. Amer. Chem. Soc.*, 1950, **72**, 2788; 1952, **74**, 664.
[33] Gilman and Van Ess, *J. Amer. Chem. Soc.*, 1939, **61**, 1365.
[34] Buu-Hoï and Royer, *Rec. Trav. chim.*, 1948, **67**, 175.
[35] Gilman and Avakian, *J. Amer. Chem. Soc.*, 1946, **68**, 580.
[36] Gilman and Wilder, *J. Amer. Chem. Soc.*, 1954, **76**, 2906.
[37] Gilman and Wilder, *J. Org. Chem.*, 1957, **22**, 523.
[38] Illuminati, Nobis, and Gilman, *J. Amer. Chem. Soc.*, 1951, **73**, 5887.
[39] Gilman and Nobis, *J. Amer. Chem. Soc.*, 1950, **72**, 2629.

Rate Measurements.—Reaction mixtures consisted of 2 ml. of aqueous perchloric acid (of strength shown in the Table) and 5 ml. of a solution of organosilane in methanol (usually 2—10 mg./50 ml.). Rates at 50·00° ± 0·03° were measured as previously described, some " infinite time " values of the optical density being measured on samples kept in sealed tubes.[2,3,27] Rate-constants could be duplicated to within ±1%.

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THE UNIVERSITY, LEICESTER. [*Received, May 18th*, 1961.]

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969. *Aromatic Reactivity. Part XIX.*[1] *Detritiation of* [o- *and* p-$^3H_1$]-*Toluene and -t-Butylbenzene.*

By R. BAKER, C. EABORN, and R. TAYLOR.

The reactivity of *o*- relative to that of *p*-tritiotoluene in detritiation varies markedly with the medium (*e.g.*, the reactivity ratio is 1·05 in 74·8% sulphuric acid at 25°, 0·49 in anhydrous trifluoroacetic acid at 70°, and 0·39 in anhydrous heptafluorobutyric acid at 70°). The relative reactivities of *o*- and *p*-tritio-t-butylbenzene vary in a closely similar way, and so the effect cannot originate in steric hindrance by the *o*-alkyl groups. It is suggested that in this and other electrophilic substitutions, activation of an *ortho*- relative to that of a *para*-position by an alkyl group may depend upon the nature of the electrophile, possibly increasing with increasing reactivity of the latter.

THE relative reactivities of the *ortho*- and *para*-positions of toluene in hydrogen-exchange seem to vary considerably as the medium is varied. Thus the following ratios, f_o/f_p, of the rate factors applying to these positions have been reported: 1·11 for tritiation in 80·8% aqueous sulphuric acid,[2] 1·09 for dedeuteration in 70·8% aqueous perchloric acid,[3] 1·00 for dedeuteration in 68% aqueous sulphuric acid,[4] 0·95 for deuteration in 50 mole-% sulphuric acid,[5] 0·70 for deuteration in trifluoroacetic acid containing a little sulphuric acid,[6] 0·60 for deuteration in *ca.* 95 vol.-% aqueous trifluoroacetic acid,[5] 0·41 for dedeuteration in anhydrous heptafluorobutyric acid,[3] and 0·17 for deuteration in liquid deuterium bromide.[7]

It is usual to explain f_o/f_p ratios for electrophilic substitution in toluene in terms of steric hindrance, and Tiers suggested as a possible explanation of the smallness of the ratio in hydrogen-exchange in heptafluorobutyric acid the larger steric requirements of the proton donor compared with those in aqueous perchloric acid.[3] As an alternative, Lauer, Matson, and Stedman [5] suggested that steric hindrance to solvation for reaction at the *ortho*- relative to that at the *para*-position might be smaller in sulphuric acid than in trifluoroacetic or heptafluorobutyric acid, although it is more likely that steric hindrance to solvation by the *o*-methyl group would be relatively *less* important in the more weakly solvating media (cf. ref. 8).

Again, from the magnitude of the f_o/f_p ratio in dedeuteration in 68% aqueous sulphuric

[1] Part XVIII, Eaborn and Sperry, preceding paper.
[2] Melander and Olsson, *Acta Chem. Scand.*, 1956, **10**, 879.
[3] Tiers, *J. Amer. Chem. Soc.*, 1956, **78**, 4165.
[4] Gold and Satchell, *J.*, 1956, 2743.
[5] Lauer, Matson, and Stedman, *J. Amer. Chem. Soc.*, 1958, **80**, 6433.
[6] Mackor, Smit, and van der Waals, *Trans. Faraday Soc.*, 1957, **53**, 1309.
[7] Shatenshtein, Kalenachenko, and Varshavskii, *Zhur. fiz. Khim.*, 1956, **30**, 2098.
[8] Eaborn and Taylor, *J.*, 1961, 247.

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acid compared with the ratios in ionic bromination [9] and nitronium-ion nitration [10] (*viz.*, 1·29 and 0·72, respectively), Gold and Satchell inferred that the attacking species in the dedeuteration is larger than that in the bromination,[4] although such an inference is, in our opinion, inconsistent with their mechanism for the exchange process. In this " unorthodox " mechanism,* a fast proton-transfer from the acid to the aromatic compound gives an " outer " complex, and the hydrogen exchange occurs in a slow rearrangement of this complex.[4,11] The rate-determining transition state contains only the aromatic species and a proton, free from solvent, and it is difficult to believe that the steric requirements of this proton would be larger than that of the bromonium ion. Any evidence of marked variation in steric hindrance by an *o*-methyl group with change in the catalysing acid, HA, would argue strongly against the mechanism, since the conjugate base A is absent in the rate-determining transition state and cannot exercise any direct influence on it.

To throw light on the importance of steric effects in hydrogen-exchange we have measured the rates of detritiation of [*o*- and *p*-$^3H_1$]-toluene and -t-butylbenzene in several media; if variation in the f_o/f_p ratio in toluene arises from steric hindrance, either by compression between the methyl group and the incoming and outgoing groups at the reaction centre, or by interference with solvation, then the effect should be much greater in t-butylbenzene. The results, listed in the Table, show that the f_o/f_p ratio varies in precisely the same way for toluene and t-butylbenzene, being slightly lower for the latter throughout. The variations must thus arise from the polar influences of the alkyl groups.

Detritiation of X·C_6H_4·^3H compounds.

(i) Medium: H_2SO_4–H_2O. Temperature: 24·84°.

$[H_2SO_4]$ [a]	10^7k (sec.$^{-1}$) [b]		f_o/f_p	$[H_2SO_4]$ [a]	10^7k (sec.$^{-1}$) [b]		f_o/f_p
	X = *o*-Me	*p*-Me			X = *o*-Me	*p*-Me	
74·85	5185	4915	1·055	69·00	316	320	0·99
73·25	2800	2710	1·04	64·50	49·6	50·7	0·98
70·70	753	753	1·00				
					X = *o*-Bu^t	*p*-Bu^t	
				71·41	768	805	0·955

(ii) Temperature: 70·11°

Medium	10^7k (sec.$^{-1}$) X = *o*-Me	*p*-Me	*o*-Bu^t	*p*-Bu^t	f_o^{Me}/f_p^{Me}	$f_o^{Bu^t}/f_p^{Bu^t}$
CF_3·CO_2H–H_2O–$HClO_4$ [c,d] (92·04)–(5·45)–(2·51)	330	313	393	387	1·05	1·02
CF_3·CO_2H–H_2O–H_2SO_4 [c,d] (93·00)–(5·12)–(1·88)	1295	1770	1565	2180	0·73	0·72
CF_3·CO_2H	20·8	42·7	23·0	50·9	0·49	0·45
n-C_3F_7·CO_2H	2·79	7·08	3·34	8·94	0·39	0·37

[a] Wt.-%. [b] No corrections for sulphonation have been applied since they would be small, and identical for *ortho*- and *para*-isomers. [c] These results are from Eaborn and Taylor, *J.*, 1961, 247. [d] Figures in parentheses denote mole-%.

The fall in the f_o/f_p ratio parallels the fall in the dielectric constant of the medium. Electrostatic repulsion between the partial positive charges on the hydrogen atoms of the alkyl group and the positive charge at the reaction centre will be greater in media of low dielectric constant, and might be expected to contribute to the smallness of the f_o/f_p ratios, but if this were a major effect it would be much more marked with the t-butyl than with

* For the meaning of the descriptions " orthodox " and " unorthodox " in this context see refs. 8 and 12.

[9] de la Mare and Harvey, *J.*, 1956, 36.
[10] Cohn, Hughes, Jones, and Peeling, *Nature*, 1952, **169**, 291; cf. Knowles, Norman, and Radda, *J.*, 1960, 4885.
[11] Gold and Satchell, *J.*, 1955, 3609, 3619, 3622; Gold, Lambert, and Satchell, *Chem. and Ind.*, 1959, 1312.
[12] Kresge and Chiang, *Proc. Chem. Soc.*, 1961, 81.

the methyl group. The most likely explanation of the variations is that the polar effect of an *o*- relative to that of a *p*-alkyl group varies with the electron-demand of the attacking electrophile, and our results are consistent with associating the decrease in the f_o/f_p ratios with decreasing acidity and reactivity of the attacking acid. It is reasonable to assume that inductive effects of alkyl groups reach *ortho*- more effectively than *para*-positions, but that their tautomeric effects (or polarizability effects, in general) reach the *para*-position more easily (just as the $+T$ effects of OR and NR_2 groups activate *para*- more than *ortho*-positions [13]). A decrease in the reactivity of the attacking acid will be accompanied by increasing demand on polarizability effects, and thus the f_o/f_p ratio can be expected to fall.* Alternatively the high f_o/f_p ratios may be associated with positively charged, and the low ratios with neutral, attacking species (*e.g.*, the un-ionized acids, $CF_3{\cdot}CO_2H$, $C_3F_7{\cdot}CO_2H$, and DBr), and it is noteworthy that, in chlorination, for example, the ratio is higher for attack by the chloronium ion or related species ($f_o/f_p = 1{\cdot}63$) than for attack by molecular chlorine ($f_o/f_p = 0{\cdot}75$).[16] (Steric factors probably play some part in molecular chlorination, however, but possibly not a large one in the case of toluene, since the f_o^{But}/f_p^{But} ratio is only five times smaller than the f_o^{Me}/f_p^{Me} ratio.[16]) However, the greater electron-demand usually shown by neutral than by positively charged electrophiles is probably itself a result of the greater reactivity of the positively charged species.

It will be realised that whatever the explanation of our results they have a general significance for interpretation of f_o/f_p ratios in electrophilic substitutions in alkylbenzenes, since these can no longer necessarily be attributed wholly or even mainly to steric effects. Thus it is no longer justifiable to use the f_o/f_p ratios in ionic chlorination and bromination of toluene (1·63 and 1·29, respectively) to conclude that the steric requirements of the former reaction are smaller [16] (although they probably are), for it is likely that the steric effect is small in both bases and that the lower ratio in bromination is associated with the greater stability, and thus lower reactivity, of the bromonium ion. Similarly, it cannot be concluded from the f_o/f_p ratios in toluene that the steric requirements of hydrogen exchange in aqueous sulphuric acid are intermediate between those in ionic bromination and nitration, as has been suggested.[4] We suggest that only when a low f_o/f_p ratio for toluene is accompanied by a markedly smaller ratio for t-butylbenzene is it reasonable to conclude that steric hindrance to *ortho*-substitution is probably important in t-butylbenzene, and possibly of significance also in toluene.

Our results are, we believe, more easily reconciled with the " orthodox " than with the " unorthodox " mechanism of hydrogen exchange. In the former the conjugate base A of the catalysing acid HA is covalently involved in the highest-energy transition state(s) and thus can influence the electron demand directly, so that the variations in the f_o/f_p ratio become understandable in terms of the chemical properties of the acid HA, as we have indicated above. In the " unorthodox " mechanism, the residue A is not covalently involved in the highest-energy transition state(s), and the effect on the f_o/f_p ratios of changing the acid would have to be explained either in terms of general solvent effects (which would be difficult) or by introducing the complication of postulating changes in mechanism with changes of acid.

The increase in the f_o/f_p ratio for toluene with increasing concentration of aqueous

* From medium to medium the value of f_p^{Me} in hydrogen exchange is not a wholly reliable measure of the demand on polarizability effects,[5, 14] but the highest values of the f_o/f_p ratio for toluene, those in trifluoroacetic acid containing perchloric acid and those in aqueous sulphuric acid, are associated with the smallest values of f_p^{Me} (*viz.*, 313 [6] and 250,[15] respectively) while the intermediate values of the ratio correspond with intermediate values of f_p^{Me} (in anhydrous trifluoroacetic acid, $f_p^{Me} = 450$), and the lowest value of the ratio, that in anhydrous deuterium bromide, is associated with an exceptionally large value of f_p^{Me} (*viz.*, 6000).[7]

[13] de la Mare and Ridd, " Aromatic Substitution. Nitration and Halogenation," Butterworths Scientific Publ., London, 1959, pp. 145—146.
[14] Eaborn and Taylor, *J.*, 1961, 2388.
[15] Eaborn and Taylor, *J.*, 1960, 3301.
[16] Ref. 13, pp. 142—144.

sulphuric acid is probably real, and this would agree with the few results previously reported separately for particular concentrations.[2-5] It is noteworthy that, while the hyperconjugative order of activation, *o*-Me > *o*-Bu^t, applies in aqueous sulphuric acid, the inductive order, *o*-Bu^t > *o*-Me applies in trifluoroacetic acid, alone or containing aqueous sulphuric or perchloric acid, the type and magnitude of the change being very similar to those noted previously for the *p*-alkyl groups. As one possible explanation in the case of the *para*-substituents it was suggested that the direct-field component of the inductive effect might be larger in media of low dielectric constant, so that the inductive order might apply.[8] Such an effect would, however, be much larger with the *ortho*-groups; and, since it is not, the suggestion is invalid.

Experimental

Materials.—Preparation of the tritiated aromatic compounds has been described.[8,15]

Anhydrous trifluoroacetic acid was prepared by fractionally distilling the Eastman " White Label " acid first from sulphuric acid and then from silver trifluoroacetate. Alkali titration showed it to be 100·0% pure, and Karl Fischer titration, in presence of excess of pyridine, showed it to contain <0·01% of water.

Anhydrous heptafluorobutyric acid was prepared analogously.

Rate Measurements.—The techniques were as previously described.[8,14,15]

We thank the Royal Society for the loan of apparatus from the Government Grant in Aid, and the Department of Scientific and Industrial Research for financial assistance and for a maintenance grant (to R. B.).

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970. *Reactions of Some Substituted Benzo-1,2,3-triazines.*

By E. W. Parnell.

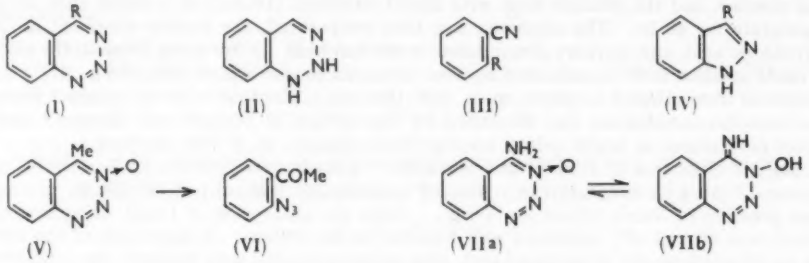
The product obtained from the diazotisation of *o*-aminobenzamidoxime is not the hydroxylamine (I; R = NH·OH), but is probably 4-aminobenzo-1,2,3-triazine 3-oxide (VIIa). The reactions of 4-hydrazinobenzo-1,2,3-triazine with copper salts have been studied.

A compound alleged to be the hydroxylamine (I; R = NH·OH) was first prepared by diazotisation of *o*-aminobenzamidoxime by Pinnow and Sämann.[1] When reduced with stannous chloride it gave a base, $C_7H_7N_3$, which was formulated as 1,2-dihydrobenzo-1,2,3-triazine (II). Gabriel[2] obtained this compound by diazotisation and reduction of *o*-aminobenzonitrile and assigned to it the structure (III; R = NH·NH$_2$), but recently Aron and Elvidge,[3] and Cooper,[4] have shown that the product from both reactions is in fact 3-aminoindazole (IV; R = NH$_2$).

The " hydroxylamine " of Pinnow and Sämann[1] has now been reduced catalytically (Raney nickel), giving ammonia, *o*-aminobenzonitrile (III; R = NH$_2$), and 3-aminoindazole (IV; R = NH$_2$). Grundmann and Ulrich[5] noted that reduction of the corresponding 7-chloro-derivative by sodium borohydride yielded only 2-amino-4-chlorobenzonitrile. A novel transformation of the " hydroxylamine " has also been observed on fusion with ammonium acetate; *o*-azidobenzonitrile (III; R = N$_3$) was formed in high yield. The reduction of the " hydroxylamine " to 3-aminoindazole, and the conversion into the azide, closely resemble the reactions of 4-methylbenzo-1,2,3-triazine 3-oxide (V),

[1] Pinnow and Sämann, *Ber.*, 1896, **29**, 623.
[2] Gabriel, *Ber.*, 1903, **36**, 805.
[3] Aron and Elvidge, *Chem. and Ind.*, 1958, **38**, 1234.
[4] Cooper, *J.*, 1958, 4212.
[5] Grundmann and Ulrich, *J. Org. Chem.*, 1959, **24**, 272.

prepared by Meisenheimer, Senn, and Zimmermann [6] by diazotisation of *o*-aminoacetophenone oxime. In this instance reduction gave 3-methylindazole (IV; R = Me) and treatment with dilute sulphuric acid or a mixture of phosphorus tri- and penta-chloride gave *o*-azidoacetophenone (VI). These similarities suggested that Pinnow and Sämann's compound might be the *N*-oxide (VIIa) or its tautomer (VIIb). Further evidence was



obtained by treatment of the thiol (I; R = SH) with hydroxylamine, affording the authentic compound (I; R = NH·OH). This differed in physical properties and ultraviolet and infrared absorption spectra from Pinnow and Sämann's compound, which therefore in all probability has structure (VII). The compounds prepared by Grundmann and Ulrich [5] from 2-amino-4-chloro- and 2-amino-4-methoxy-benzamidoximes must hence be derivatives of (VII).

The compounds (I; R = NH_2 and R = NH·NH_2) have previously been prepared [5] from the methylthio-derivative (I; R = SMe). They have now been obtained directly from the thiol (I; R = SH); and the amine (I; R = NH_2) has been made by diazotisation of *o*-aminobenzamidine.

In an attempt to prepare the unknown parent base, benzo-1,2,3-triazine, the 4-hydrazino-compound was heated with aqueous cupric sulphate; [7] nitrogen was evolved but only benzaldehyde and salicylonitrile were isolated. The nitrile is probably formed by hydrolysis of a *o*-cyanobenzenediazonium salt (cf. Buckley and Gibson [8]) and this is in agreement with the many observations [9] that benzo-1,2,3-triazines often behave as diazonium salts. The formation of benzaldehyde may be explained by oxidation of the hydrazine (I; R = NH·NH_2) to benzo-1,2,3-triazine, (I; R = H), ring fission to a benzaldimine-*o*-diazonium salt, reduction by hydrazine,[10] and finally hydrolysis to benzaldehyde. These two schemes suggested that in the presence of cuprous chloride *o*-chlorobenzonitrile and *o*-chlorobenzaldehyde might be formed. This was so; about 40% of the nitrile and a trace of aldehyde were produced. Benzo-1,2,3-triazine could not be isolated from any of these reactions.

Experimental

4-Aminobenzo-1,2,3-triazine.—(*a*) *o*-Aminobenzamidine dihydrochloride [11] (2·0 g.), dissolved in water (10 ml.) and 2N-hydrochloric acid (5 ml.), was treated at 0° with sodium nitrite (0·73 g.) in water (3 ml.). A solid soon separated and was redissolved by warming the mixture to 20° and diluting it with water. Addition of concentrated aqueous ammonia gave the crude product (1·3 g., quant.), m. p. 254—260° (decomp.), which crystallised from ethanol as pale yellow plates,[12] m. p. 266° (decomp.) (Found: C, 57·5; H, 4·4; N, 39·0. Calc. for $C_7H_6N_4$: C, 57·5;

[6] Meisenheimer, Senn, and Zimmermann, *Ber.*, 1927, **60**, 1736.
[7] Schofield and Swain, *J.*, 1950, 392.
[8] Buckley and Gibson, *J.*, 1956, 3242.
[9] Erickson, Wiley, and Wystrach (1956). "The 1,2,3- and 1,2,4-triazines, tetrazines, and pentazines," New York, Wiley.
[10] Hantzsch and Vock, *Ber.*, 1903, **36**, 2066.
[11] Carrington, *J.*, 1955, 2527.
[12] The m. p.s of the benzo-1,2,3-triazines vary greatly with the rate of heating.

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H, 4·1; N, 38·4%). The *picrate*, yellow prisms from water, had m. p. 237—238° (decomp.) (Found: N, 26·1. $C_7H_6N_4,C_6H_3N_3O_7$ requires N, 26·2%). The amino-compound evolved nitrogen when warmed with aqueous sodium hydroxide. Treatment with methyl iodide in methanol gave a *methiodide* as slender yellow needles (from ethanol), m. p. 216—217° (decomp.) (Found: N, 19·1; I, 43·8. $C_8H_9IN_4$ requires N, 19·4; I, 44·1%).

(*b*) 4-Mercaptobenzo-1,2,3-triazine [2] (1·0 g.) was ground with mercuric chloride (2·5 g.) to a fine powder, and the mixture kept with liquid ammonia (10 ml.) in a sealed tube at room temperature for 48 hr. The ammonia was then evaporated, the residue dissolved in dilute hydrochloric acid, and mercury precipitated as the sulphide. After being filtered, the solution was made alkaline with concentrated aqueous ammonia to give a pink solid (0·6 g., 67%) which crystallised from ethanol as plates, m. p. 266° (decomp.), identical with the product from (*a*).

o-Aminobenzamidoxime was diazotised by the method of Pinnow and Sämann [2] and the product crystallised as bright yellow needles (from ethanol), m. p. 191° (decomp.).

Catalytic Reduction of Pinnow and Sämann's " 4-*Hydroxyaminobenzo*-1,2,3-*triazine."*—The compound [2] (10 g.) was catalytically reduced in methanol (100 ml.) at 60°/400 lb. per sq. in. in the presence of Raney nickel (*ca.* 1·0 g.). After the absorption of 1 mol. of hydrogen the catalyst was filtered off; ammonia was detected in the filtrate. Evaporation of the solvent gave an oil which slowly crystallised and, after being triturated with benzene, the solid (2·0 g.) was crystallised from propan-2-ol and then from benzene to give 3-aminoindazole, m. p. 157—158° (Found: C, 62·8; H, 5·6; N, 32·7. Calc. for $C_7H_7N_3$: C, 63·2; H, 5·3; N, 31·6%). *o*-Aminobenzonitrile was also isolated as the hydrochloride, m. p. 197° (decomp.), from the oily reduction product (Found: C, 53·7; H, 4·4; Cl, 22·6; N, 18·2. Calc. for $C_7H_6N_2,HCl$: C, 54·3; H, 4·5; Cl, 23·0; N, 18·1%).

Fusion of " 4-*Hydroxyaminobenzo*-1,2,3-*triazine" with Ammonium Acetate.*—The compound [2] (1·0 g.) and ammonium acetate (5·0 g.) were heated at 135° during 5 min. The yellow colour of the starting material faded and an oil separated from the melt. After a further 3 min. the mixture was cooled and water (10 ml.) added. The oil solidified and was filtered off. Crystallisation of this solid (0·75 g., 84%) from light petroleum gave pure *o*-azidobenzonitrile, m. p. 54—55° (Found: C, 57·8; H, 2·76; N, 39·7. Calc. for $C_7H_4N_4$: C, 58·2; H, 2·78; N, 38·9%).

4-*Hydrazinobenzo*-1,2,3-*triazine.*—4-Mercaptobenzo-1,2,3-triazine (26 g.) was added to hydrazine hydrate (130 ml.; 60% w/v solution) cooled in ice. Hydrogen sulphide was evolved, the solid dissolved, and the product separated and after 16 hr. at room temperature was filtered off. The crude product (21 g.), m. p. 186° (decomp.), crystallised from methanol as brown needles, m. p. 188° (decomp.) (Found: C, 52·0; H, 4·0; N, 43·8. Calc. for $C_7H_7N_5$: C, 52·2; H, 4·35; N, 43·5%). The *methanesulphonate* crystallised from methanol–ether as silvery plates, m. p. 166—167° (decomp.) (Found: N, 27·0; S, 12·8. $C_7H_7N_5,CH_4O_3S$ requires N, 27·2; S, 12·4%).

Authentic 4-*Hydroxyaminobenzo*-1,2,3-*triazine.*—4-Mercaptobenzo-1,2,3-triazine (2·0 g.), hydroxylamine hydrochloride (0·94 g.), sodium acetate (1·1 g.), and ethanol (40 ml.) were refluxed together overnight. The hot mixture was filtered, the filtrate evaporated to low bulk, and the residue triturated with water. Crystallisation of the residue (1·45 g., 73%), m. p. 170° (decomp.), from aqueous methanol or nitromethane gave the pure compound as fine cream-coloured needles, m. p. 175° (decomp.) (Found: C, 52·0; H, 4·0; N, 34·0. Calc. for $C_7H_6N_4O$: C, 51·9; H, 3·7; N, 34·0%).

Reaction of 4-*Hydrazinobenzo*-1,2,3-*triazine with Cupric Sulphate.*—4-Hydrazinobenzo-1,2,3-triazine methanesulphonate (1·0 g.), dissolved in water (5 ml.), was added to cupric sulphate pentahydrate (10 g.), dissolved in water (45 ml.). The resultant suspension was boiled, and distilled until the distillate was clear (*ca.* 5 min.). The oil isolated from the distillate was neutral and was converted into its 2,4-dinitrophenylhydrazone (50 mg.) which, crystallised from acetic acid, had m. p. 243°, undepressed by admixture with benzaldehyde 2,4-dinitrophenylhydrazone. The residual reaction solution was extracted with ether, and the phenolic component isolated from the extract by alkali as a solid (*ca.* 20 mg.), m. p. 87—91°. This crystallised from light petroleum (b. p. 60—80°), and had m. p. 93—95°, undepressed by authentic salicylonitrile.

Reaction of 4-*Hydrazinobenzo*-1,2,3-*triazine and Cupric Chloride.–Cuprous Chloride.*—4-Hydrazinobenzo-1,2,3-triazine methanesulphonate (1·0 g.), in water (5 ml.), was added to cupric sulphate pentahydrate (10 g.), cuprous chloride (1·0 g.), and concentrated hydrochloric acid (10 ml.), in water (40 ml.). The resultant suspension was boiled and distilled until no more solid distilled with the steam. The solid, *o*-chlorobenzonitrile (0·25 g.), m. p. 40—42°,

crystallised from light petroleum (b. p. 40—60°) and then had m. p. and mixed m. p. 42—43°. The residual reaction solution was extracted with ether, yielding a trace of oil which gave *o*-chlorobenzaldehyde 2,4-dinitrophenylhydrazone (*ca.* 10 mg.), m. p. and mixed m. p. 211° (from acetic acid).

The author thanks Dr. J. N. Ashley, F.R.I.C., for his active interest in this work, Mr. S. Bance, B.Sc., F.R.I.C., for the microanalyses, and Dr. D. F. Muggleton for the spectroscopic measurements.

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971. *The Reactions of Hexamethyldisilthiane and Ethylthiotrimethylsilane with Alcohols, Thiols, Acids, and Amines.*

By E. W. ABEL.

Hexamethyldisilthiane, $S(SiMe_3)_2$, has been prepared in good yield from anhydrous sodium sulphide and chlorotrimethylsilane. The reactions of hexamethyldisilthiane with alcohols, thiols, acids, and amines have been investigated. From these reactions the series of compounds $R{\cdot}SiMe_3$ where R = EtO, Bu^nO, Pr^iO, Bu^tO, Bu^nS, Et·CO·O, BzO, Bu^n_2N, $Bu^n{\cdot}NH$, Ph·NH was produced. Similarly, reactions of ethylthiotrimethylsilane with the requisite amine and acid have given in each case ethanethiol and $R{\cdot}SiMe_3$ where R = Et·CO·O, BzO, Bu^n_2N, $Bu^n{\cdot}NH$, Ph·NH.

PREVIOUSLY, the formation of the alkyldisilthianes from alkylsilicon halides has involved [1-3] the expensive iodides and silver sulphide. It is now found that chlorotrimethylsilane and anhydrous sodium sulphide give almost quantitative yields of hexamethyldisilthiane, $S(SiMe_3)_2$. The reaction did not take place under ordinary conditions of temperature and pressure, but proceeded smoothly in pressure vessels at 250°:

$$2Me_3SiCl + Na_2S \longrightarrow (Me_3Si)_2S + 2NaCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The Si–S bond has been shown [2] to be readily attacked by water; also alcoholysis of the alkythiotrimethylsilanes produced [4] alkoxytrimethylsilanes. A number of these alkoxytrimethylsilanes have now been prepared by alcoholysis of hexamethyldisilthiane:

$$(Me_3Si)_2S + ROH \longrightarrow Me_3Si{\cdot}SH + RO{\cdot}SiMe_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$Me_3Si{\cdot}SH + ROH \longrightarrow H_2S + RO{\cdot}SiMe_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The reaction was exothermic in the cases of ethanol and butan-1-ol, and high yields of the corresponding alkoxytrimethylsilanes were obtained. In the cases of propan-2-ol and t-butyl alcohol, however, the reaction required heating and was slow, and yields were not as good. The reaction is written in two stages (2 and 3), with the initial formation of trimethylsilanethiol, as when heating was necessary the temperature of reflux invariably remained at 77—78° for some time. Although the thiol [5] was not isolated as such, this temperature suggested its presence (b. p. 77°), and it would then react with further alcohol.

In the corresponding reactions of hexamethyldisilthiane with thiols, hydrogen sulphide was evolved only slowly upon prolonged refluxing, and owing to the very long times required reactions were not carried to completion. The alkylthiotrimethylsilanes were

[1] Eaborn, *Nature*, 1950, **165**, 685.
[2] Eaborn, *J.*, 1950, 3077.
[3] Emeléus, Onyszchuk, and Kuchen, *Z. anorg. Chem.*, 1956, **283**, 74.
[4] Abel, *J.*, 1960, 4406.
[5] Larsson and Marin, *Acta Chem. Scand.*, 1951, **5**, 964.

isolated in varying yields. 1,1-Dimethylethanethiol did not react with hexamethyldisilthiane.

The reactions of hydrogen sulphide [5-7] and thiols [4,6] with aminosilanes have been extensively studied for the production of Si–S from Si–N bonds. As a result of the approximately equal replacement tendencies of the alkylthio- and alkylamino-groups in these and similar [8] systems, the reverse procedure has now been used to produce aminosilanes from compounds containing Si–S bonds. Hexamethyldisilthiane, when heated with di-n-butylamine, n-butylamine, or aniline evolved hydrogen sulphide, and produced, respectively, di-n-butylamino-, butylamino-, and anilino-trimethylsilane:

$$2R_2NH + (Me_3Si)_2S \longrightarrow H_2S + 2R_2N{\cdot}SiMe_3 \quad (4)$$

$$2R{\cdot}NH_2 + (Me_3Si)_2S \longrightarrow H_2S + 2R{\cdot}NH{\cdot}SiMe_3 \quad (5)$$

The reactions were slow, and yields of aminosilanes were not good. Although expressions (4) and (5) are written to represent the overall reaction, again trimethylsilanethiol appeared to be present, and possibly as a result of its slightly acidic nature, formed compounds with the amines present. Similar reactions between these amines and ethylthiotrimethylsilane gave ethanethiol and the same aminosilanes:

$$R_2NH + Me_3Si{\cdot}SEt \longrightarrow EtSH + R_2N{\cdot}SiMe_3 \quad (6)$$

$$R{\cdot}NH_2 + Me_3Si{\cdot}SEt \longrightarrow EtSH + R{\cdot}NH{\cdot}SiMe_3 \quad (7)$$

Propionic acid and hexamethyldisilthiane did not react in the cold but, on warming, hydrogen sulphide was evolved and trimethylsilyl propionate was formed in good yield. The ester was also produced by the action of the acid on ethylthiotrimethylsilane:

$$R{\cdot}CO_2H + (Me_3Si)_2S \longrightarrow H_2S + 2R{\cdot}CO_2{\cdot}SiMe_3 \quad (8)$$

$$R{\cdot}CO_2H + Me_3Si{\cdot}SEt \longrightarrow EtSH + R{\cdot}CO_2{\cdot}SiMe_3 \quad (9)$$

Reactions (8) and (9) were also carried out with benzoic acid, giving good yields of trimethylsilyl benzoate.

In general, it may be concluded that compounds containing Si–S bonds react smoothly with alcohols and acids to give good yields of the products, but reactions with thiols and amines are not undergone so readily and yields of the resulting compounds are not always good.

Experimental

The reactions were carried out under anhydrous conditions with dried materials. The use of wet reagents produced hexamethyldisiloxane as a major by-product. Ethylthiotrimethylsilane was prepared as previously described,[4] and sodium sulphide was dried at 200°/0·01 mm.

Preparation of Hexamethyldisilthiane.—Anhydrous sodium sulphide (18·0 g., 1 mol.) and chlorotrimethylsilane (50·2 g., 2 mols.) were heated (20 hr.) in a heavy-walled sealed glass tube at 240°. Subsequent distillation yielded hexamethyldisilthiane (39·4 g., 96%), b. p. 163°, n_D^{20} 1·4572 (Found: C, 40·1; H, 10·6. Calc. for $C_6H_{18}SSi_2$: C, 40·4; H, 10·2%), and a dark residue of sodium chloride.

Interaction of Hexamethyldisilthiane with Alcohols.—The alcohol (0·2 mole) was added to the hexamethyldisilthiane (0·1 mole) with shaking. With ethanol and butan-1-ol, the mixture became warm and hydrogen sulphide was immediately evolved; no observable reaction took place with propan-2-ol or t-butyl alcohol. The mixture was refluxed and hydrogen sulphide was evolved in all cases. Subsequent fractionation gave varying yields of the alkoxytrimethylsilanes (see Table). These were characterised by b. p., n, and identity of the infrared spectra with those previously reported.[4]

[6] Larsson and Marin, Swed. P., 138,357/1952 (*Chem. Abs.*, 1954, **48**, 2761).
[7] Larsson and Mjörne, *Acta Chem. Scand.*, 1951, **5**, 64.
[8] Aubrey and Lappert, *Proc. Chem. Soc.*, 1960, 148.

R in $Me_3Si{\cdot}OR$	Yield (%)	Reaction time (hr.)	B. p.	n_D^{20}	R in $Me_3Si{\cdot}OR$	Yield (%)	Reaction time (hr.)	B. p.	n_D^{20}
Et	92	1	75°	1·3745	Pr^i	78	15	88°	1·3788
Bu^n	94	1	125	1·3930	Bu^t	58	400	105	1·3910

Interaction of Hexamethyldisilthiane with Butane-1-thiol.—No evolution of gas occurred when the thiol (5·48 g., 2 mol.) was mixed with the hexamethyldisilthiane (5·43 g., 1 mol.) in the cold. On warming, hydrogen sulphide was evolved for 20 hr. Fractionation of the resulting oil gave n-butylthiotrimethylsilane (7·24 g., 76%), b. p. 169°, n_D^{20} 1·4553, having an authentic infrared spectrum.[4]

In a similar experiment involving hexa-1,1-dimethylethanethiol no evolution of hydrogen sulphide was noted after three days' heating, and subsequent distillation gave virtually complete recovery of the reactants.

Interaction of Hexamethyldisilthiane and Di-n-butylamine.—The amine (12·8 g., 2 mol.) and hexamethyldisilthiane (8·80 g., 1 mol.) did not evolve hydrogen sulphide when mixed, but did so when heated. After refluxing (3 days), distillation gave a large forerun of unchanged amine and the disilthiane, followed by *di-n-butylaminotrimethylsilane* (9·80 g., 49%), b. p. 200°, n_D^{20} 1·4291 (Found: C, 65·9; H, 13·7; N, 7·0. $C_{11}H_{27}NSi$ requires C, 65·7; H, 13·4; N, 7·0%).

Interaction of Hexamethyldisilthiane and n-Butylamine.—Adding the amine (8·97 g., 2 mol.) to hexamethyldisilthiane (10·95 g., 1 mol.) produced slight heating and a yellow colour. Subsequent refluxing (25 hr.) caused steady but slow evolution of hydrogen sulphide. Careful fractionation of the resulting mixture produced mainly unchanged amine and hexamethyldisilthiane, but a small quantity of butylaminotrimethylsilane [9] (2·3 g., 13%), b. p. 135°, n_D^{20} 1·4097 (Found: N, 9·71. Calc. for $C_7H_{19}NSi$: N, 9·66%), was obtained.

Interaction of Aniline and Hexamethyldisilthiane.—The amine (5·43 g., 2 mol.) and the silthiane (5·19 g., 1 mol.) did not react in the cold, but hydrogen sulphide was evolved on warming. Refluxing (25 hr.) gave hydrogen sulphide, and subsequent fractionation gave anilinotrimethylsilane [10] (8·18 g., 85%), b. p. 208°, n_D^{20} 1·5222 (Found: N, 8·6. Calc. for $C_9H_{15}NSi$: N, 8·5%).

Interaction of Hexamethyldisilthiane and Propionic Acid.—Addition of the acid (4·35 g., 2 mol.) to hexamethyldisilthiane caused neither heating nor evolution of hydrogen sulphide. On warming, a steady stream of the gas was evolved for 10 hr., and subsequent distillation gave *trimethylsilyl propionate* (7·30 g., 85%), b. p. 122°, n_D^{20} 1·3939 (Found: C, 49·8; H, 10·3. $C_6H_{14}O_2Si$ requires C, 49·3; H, 9·6%).

In a similar reaction benzoic acid produced trimethylsilyl benzoate (83%), b. p. 221°, n_D^{20} 1·4860.

Interaction of Di-n-butylamine and Ethylthiotrimethylsilane.—The amine (14·30 g., 1 mol.) and ethylthiotrimethylsilane (14·88 g., 1 mol.) underwent no apparent reaction in the cold. Heating under reflux (50 hr.) and subsequent fractionation gave ethanethiol (4·29 g., 62%), b. p. 35°, n_D^{20} 1·4300, a middle fraction of unchanged reactants, and finally di-n-butylaminosilane (15·1 g., 68%), b. p. 200°, n_D^{20} 1·4291 (Found: N, 6·9%).

Similar reactions of ethylthiotrimethylsilane with n-butylamine and aniline gave, respectively, butylaminotrimethylsilane (58%), b. p. 134°, n_D^{20} 1·4100 (Found: N, 9·5%), and anilinotrimethylsilane (71%), b. p. 207°, n_D^{20} 1·5222 (Found: N, 8·7%).

Interaction of Ethylthiotrimethylsilane and Propionic Acid.—The acid (3·22 g., 1 mol.) and ethylthiotrimethylsilane (5·83 g., 1 mol.) were heated together under reflux (5 hr.). Subsequent fractionation gave ethanethiol (2·29 g., 85%), b. p. 34°, n_D^{20} 1·4297, and trimethylsilyl propionate (5·72 g., 90%), b. p. 122°, n_D^{20} 1·3941 (Found: C, 49·1; H, 10·1%).

Similar use of benzoic acid gave trimethylsilyl benzoate (83%), b. p. 220°, n_D^{20} 1·4858.

A grant from the Chemical Society Research Fund, and a gift of trimethylchlorosilane from Midland Silicones Ltd., are gratefully acknowledge.

THE UNIVERSITY, BRISTOL, 8. [*Received, June 13th*, 1961.]

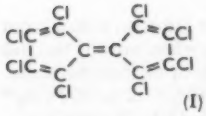
[9] Langer, Connell, and Wender, *J. Org. Chem.*, 1958, **23**, 50.
[10] Osthoff and Kantor, *Inorg. Synth.*, 1957, **5**, 55.

XUM

972. *An X-Ray Determination of the Crystal and Molecular Structure of Perchlorofulvalene.*

By P. J. Wheatley.

The crystal and molecular structure of perchlorofulvalene has been determined by two-dimensional *X*-ray diffraction methods. The two halves of the molecule are twisted through an angle of 41°. The chlorine atoms are all displaced from the plane of the five-membered ring of carbon atoms. The central C–C bond adopts a length of 1·49 Å.


(I)

The preparation and properties of perchlorofulvalene (I) have recently been described.[1] The present paper gives an account of a two-dimensional *X*-ray determination of the crystal and molecular structure.

Experimental.—$C_{10}Cl_8$. $M = 403{\cdot}8$. Monoclinic. $a = 14{\cdot}96_2$, $b = 7{\cdot}90_0$, $c = 11{\cdot}80_3$ Å, $\beta = 103°\ 33'$. $U = 1356$ Å^3. $D_m = 1{\cdot}98$ (by flotation in a mixture of ethyl iodide and 1,2-dibromoethane), $Z = 4$, $D_c = 1{\cdot}977$, $F(000) = 784$. Space group $C2/c$ (C_{2h}^6, No. 15). Cu-K_α radiation ($\lambda = 1{\cdot}542$ Å), single-crystal rotation and Weissenberg photographs.

The crystals are deep violet. Multiple-film Weissenberg photographs were taken round [*b*] and [*c*]. Relative intensities were estimated by visual comparison with standard charts prepared from the same crystals. Very small crystal fragments were used, and no correction was made for absorption ($\mu = 146{\cdot}8$ cm.$^{-1}$). 102 *h*0*l* and 74 *hk*0 reflexions were observed to be non-zero. In order to proceed with the analysis, it was assumed that the space group was $C2/c$, rather than Cc, and that the molecule could not possess a centre of symmetry because of the close approach of chlorine atoms in the two halves of the molecule, but could posses a two-fold axis. These assumptions were justified by the success of the analysis.

Sharpened Patterson syntheses were calculated for each projection, but could not be interpreted owing to the surfeit of heavy-atom vectors. Finally a suitable interpretation of the *h*0*l* zone was obtained from a consideration of the strength of the plane $\bar{2}.0.4$, monitored by the two planes 2.0.4 and 4.0.2. This projection was then refined by Fourier and difference techniques until *R* had fallen to 19%. It was then clear that no better agreement could be obtained without allowance for the anisotropic thermal motion of the chlorine atoms. Such an allowance could not be made without adequate computing facilities, and refinement was thus terminated. It was clear from the difference maps that the chlorine atoms were vibrating most freely in the plane of the ring and perpendicular to the C–Cl bonds.

In order to solve the *hk*0 projection it was assumed that the centre of the molecule would lie close to $y = 1/4$. Again this assumption was justified, and refinement proceeded smoothly until *R* had dropped to 19%; then again anisotropic thermal motion prevented further improvement. The scattering factors used were those of Berghuis *et al.*[2] for the carbon atoms, and that of Tomiie and Stam [3] for the chlorine atoms. An isotropic temperature factor $B = 2{\cdot}67$ Å^2 was used for the *h*0*l* projection, and $B = 4{\cdot}05$ Å^2 for the *hk*0 projection.

Results.—The co-ordinates of the atoms are given in Table 1, and the observed and calculated structure factors in Table 2. Figs. 1(a and b) show the final Fourier maps of the *h*0*l* and *hk*0 projections respectively. Fig. 2 shows the bond lengths, the bond angles, and the numbering of the atoms. The agreement between the lengths of the C–Cl bonds is good, the average value being 1·692 Å. The central C–C bond is increased considerably from that of a standard double bond, and is close to the length found in biphenyl (1·49 Å).[4] The increase evidently reflects a decrease in conjugation resulting from the twisting of the two halves of the molecule. The lengths of the C–C bonds in the five-membered ring

[1] Mark, *Tetrahedron Letters*, 1961, 333.
[2] Berghuis, Haanappel, Potters, Loopstra, MacGillavry, and Veenendaal, *Acta Cryst.*, 1955, **8**, 478.
[3] Tomiie and Stam, *Acta Cryst.*, 1958, **11**, 126.
[4] Almenningen and Bastiansen, *Kgl. Norske Videnskab. Selskabs Skrifter*, 1958, **4**, 1.

are in general agreement with those found in dimethylfulvene [5] if due allowance is made for the lower accuracy of the present analysis.

The five-membered ring of carbon atoms is found to be planar. The equation of the plane through C_1, C_3, and C_4 is

$$1{\cdot}0528x - 2{\cdot}8211y - 0{\cdot}0337z + 5{\cdot}9217 = 0.$$

This equation is obtained in terms of orthogonal axes in which $[b']$ and $[c']$ coincide with the original $[b]$ and $[c]$ respectively, and $[a']$ is perpendicular to $[b']$ and $[c']$. The orthogonal co-ordinates are also given in Table 1. The atoms C_2 and C_5 lie at distances 0·020 and 0·018 Å, respectively, from this plane. The angle between the planes of the rings is

TABLE 1.

Fractional co-ordinates (x/a, y/b, z/c) and orthogonal co-ordinates (X, Y, Z in Å).

Atom	x/a	y/b	z/c	X	Y	Z
Cl_1	0·166	0·406	0·415	2·415	3·207	4·316
Cl_2	0·080	0·322	0·649	1·164	2·544	7·380
Cl_3	−0·125	0·141	0·563	−1·818	1·114	7·088
Cl_4	−0·183	0·119	0·272	−2·662	0·940	3·852
C_1	−0·006	0·256	0·311	−0·087	2·022	3·692
C_2	0·067	0·302	0·414	0·975	2·386	4·652
C_3	0·028	0·276	0·509	0·407	2·180	5·910
C_4	−0·061	0·215	0·474	−0·887	1·699	5·808
C_5	−0·085	0·203	0·356	−1·236	1·604	4·500

TABLE 2.

Observed and calculated structure factors for one asymmetric unit.

hk0	F_o	F_c	hk$\bar{1}$	F_o	F_c	hk1	F_o	F_c	hk0	F_o	F_c	hk0	F_o	F_c
2.0.0	7·2	11·4	12	2·8	−1·3	8	9·1	7·8	6	5·9	4·8	15	1·6	−1·0
4	18·5	−21·3	14	3·8	4·1	10	2·5	0·5	8	11·6	−10·4	17	1·1	−2·2
6	6·6	5·1				12	2·7	5·2	10	1·2	1·5			
8	13·2	−11·5	2.0.$\bar{8}$	8·4	−8·0	14	5·4	5·3	12	9·7	6·8	2.4.0	14·4	12·6
10	1·6	1·7	4	5·2	−4·1	16	7·0	−6·6	14	1·7	−0·5	4	13·7	12·7
12	12·2	8·6	6	3·0	−2·7	18	2·7	−4·3	16	2·4	2·8	6	6·6	−6·9
14	2·1	−0·7	8	3·3	−5·6				18	1·4	−0·3	8	3·4	2·5
16	3·6	4·3	10	4·9	5·0	2.0.$\bar{8}$	11·6	10·4				10	0·9	−0·3
18	1·7	−0·5	12	3·8	5·7	4	18·3	16·3	0.2.0	22·7	−24·5	12	1·4	−0·4
						6	2·9	−4·2	4	16·0	−15·3	14	3·4	2·7
0.0.2	7·6	6·5	2.0.10	10·7	−12·9	8	12·6	−10·5	6	1·5	0·3	16	1·4	−1·7
4	6·8	−4·5	4	5·8	9·0	10	4·3	−4·3	8	1·8	1·7	1.5.0	3·8	−4·4
6	9·7	−9·1	6	4·6	5·5	12	1·8	−2·5	10	0·8	1·3	3	1·6	−1·4
8	1·6	−3·3	10	1·5	1·0	14	3·6	4·8				5	1·1	1·2
10	5·0	−4·5				16	1·9	−0·4	1.1.0	1·4	−0·9	7	2·9	4·0
12	2·3	4·9	2.0.12	2·5	1·9	18	3·9	−3·6	3	5·7	−5·4	9	1·8	−2·0
14	3·5	5·9	6	2·8	4·9				5	0·9	0·4	13	2·2	1·5
						2.0.$\bar{10}$	9·8	11·2	7	1·3	1·7	15	1·6	−2·0
2.0.2	11·5	12·2	2.0.$\bar{2}$	5·8	4·9	4	4·7	1·1	9	5·3	5·6			
4	21·0	−23·6	4	8·7	10·4	6	9·5	9·4	11	0·8	−1·7	2.6.0	2·5	3·4
6	10·3	−11·5	6	4·0	6·7	8	1·8	3·9	13	6·6	−6·1	4	2·5	−3·5
8	18·4	18·7	8	4·4	−3·8	10	6·9	−7·6	15	3·0	2·6	6	9·6	−8·7
10	3·6	−1·3	10	15·3	−15·6	12	3·7	2·3	17	1·8	1·5	8	1·0	1·1
12	7·0	−6·8	12	4·7	−4·4	14	2·7	−3·9				10	1·6	1·3
16	7·4	−5·7	14	3·8	4·8	16	5·5	−3·6	2.2.0	20·5	−21·1	12	2·4	−1·4
			16	2·3	4·3				4	2·6	−1·3	14	1·7	1·7
2.0.4	22·7	23·1	18	1·9	1·9	2.0.$\bar{12}$	3·8	−2·8	6	10·7	10·3			
4	3·3	3·4				6	2·8	−2·5	8	1·4	1·3	1.7.0	2·8	4·2
6	6·0	5·1	2.0.$\bar{4}$	39·0	−37·2	10	7·4	7·8	10	2·5	−1·9	3	3·5	−4·9
8	3·1	1·3	4	18·0	15·6	14	5·7	−4·0	14	3·4	−2·9	5	1·4	1·1
10	4·5	−3·2	6	20·4	18·3				16	1·7	−0·9	7	3·2	3·2
12	5·1	−4·3	8	2·3	−1·8	2.0.$\bar{14}$	2·6	2·8	18	1·4	1·2	11	1·2	−0·2
14	1·6	−3·8	10	6·3	6·5	4	2·3	−2·8				13	1·2	−1·2
16	2·1	2·6	12	10·5	−9·1	6	2·4	−1·0	1.3.0	1·5	1·0			
			14	7·9	−6·5	8	1·6	−3·1	3	12·3	11·4	2.8.0	1·5	−2·6
2.0.6	18·3	18·2	16	6·9	4·0	10	2·1	1·4	5	2·0	−2·7	6	3·0	4·6
4	16·2	16·6	18	5·2	−4·4				7	6·1	−7·0	8	1·2	1·4
6	16·0	−20·1				hk0			9	3·2	−3·2	10	1·6	0·6
8	2·8	−4·3	2.0.$\bar{6}$	10·5	10·9	2.0.0	8·2	11·4	11	2·2	2·6	5.9.0	1·2	−0·7
10	4·5	5·3	6	3·3	−5·3	4	16·7	−20·7	13	4·5	5·7	7	1·6	−2·2

40° 57′. The distances of the chlorine atoms from the above plane, and the angles made by the C–Cl bonds with the plane of the ring are given in Table 3. It is quite clear from Fig. 1(b) that the chlorine atoms cannot all lie in one plane, and it is found that the two atoms on one side of the ring both lie below the plane of the carbon atoms, and the two atoms on the other side lie above this plane. This may be contrasted with the situation

[5] Norman and Post, *Acta Cryst.*, 1961, **14**, 503.

TABLE 3.

Distances from the plane through atoms C_1, C_3, and C_4, and the angles made by the C–Cl bonds with this plane.

Atom	C_2	C_5	Cl_1	Cl_2	Cl_3	Cl_4
Distance (Å)	+0·020	−0·018	−0·242	−0·093	+0·208	+0·112
Angle	—	—	8° 13′	3° 09′	7° 06′	3° 48′

in C_6Cl_6 which possesses a centre of symmetry,[6] thus implying chlorine atoms lying alternately above and below the plane. A similar distribution of chlorine atoms was also assumed in the electron-diffraction work.[7] In the latter investigation it was found that the C–Cl bonds make an angle of 12° with the plane of the ring. The values obtained here are always less than this, which may be attributed to the larger Cl · · · Cl separations to be expected in a five-membered ring.

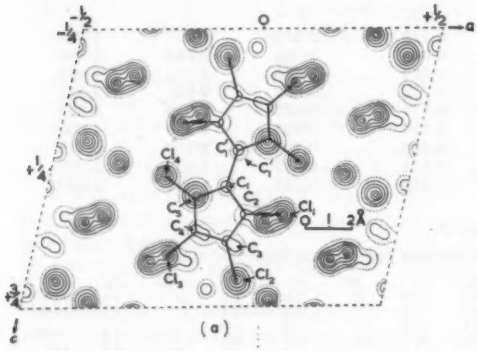


FIG. 1(a). Projection of the contents of the unit cell down [*b*].

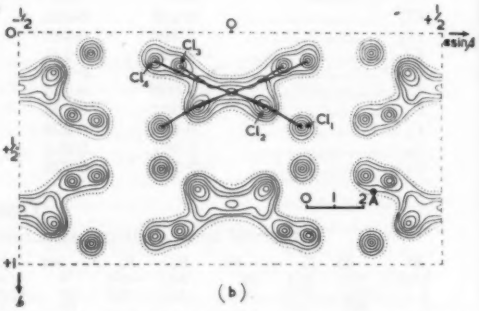


FIG. 1(b). Projection of the contents of the unit cell down [*c*].

(The contours are drawn at equal arbitrary intervals.)

The distances between non-bonded chlorine atoms all seem reasonable. The shortest distance (3·216 Å) occurs between the atoms that are responsible for the twisting of the two rings out of co-planarity. The next shortest distances (3·320, 3·344, 3·375 Å) occur between chlorine atoms attached to the same ring. There are ten distances of less than 4 Å between chlorine atoms in different molecules, the two shortest of these being 3·473 and 3·534 Å.

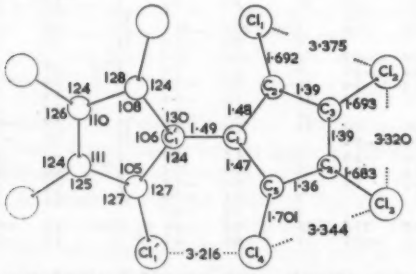


FIG. 2. The numbering of the atoms, the bond angles, and the bond lengths.

I thank Drs. A. J. Speziale and V. Mark of the Monsanto Chemical Company, St. Louis, for suggesting this problem and supplying the crystals.

MONSANTO RESEARCH S.A., BINZSTRASSE 39,
ZÜRICH 3/45, SWITZERLAND.

[*Received, June 13th*, 1961.]

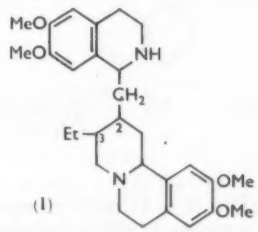
[6] Lonsdale, *Proc. Roy. Soc.*, 1931, *A*, **133**, 536.
[7] Bastiansen and Hassel, *Acta Chem. Scand.*, 1947, **1**, 489.

973. *The Synthesis of Emetine and Related Compounds. Part III.* The Reaction of Some Isoquinoline Derivatives with Acrylonitrile.*

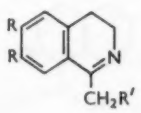
By H. T. Openshaw and Norman Whittaker.

The products of cyclisation of *N*-phenethyl-α-cyanoacetamide or its 3,4-dimethoxy-derivative with phosphoric oxide have been shown by spectroscopic methods to be the 1-cyanomethylene-1,2,3,4-tetrahydroisoquinolines (IV; R = H or OMe). Alcoholysis of these products gives the corresponding 1-ethoxycarbonylmethylene derivatives (IV; CO_2Et for CN; R = H or OMe). The salts of these bases possess the 3,4-dihydroisoquinolinium structure (IVa). Condensation of the isoquinoline (IV; R = H) with acrylonitrile gives a mono(cyanoethyl) (V) and a di(cyanoethyl) compound (VI). With alcoholic sodium ethoxide, or with toluene-*p*-sulphonic acid in toluene, the first of these is cyclised to the benzoquinolizine (VII; R = H), also formed by treatment of the second with alcoholic sodium ethoxide. Reaction of the isoquinolines (IV; R = H or OMe) with acrylonitrile in alcoholic sodium ethoxide, or of related amides (VIII; R = H or OMe) with phosphoric oxide, leads directly to the benzoquinolizine derivatives (VII; R = H or OMe). With hot aqueous acid, these quinolizines are converted into the lactams (IX; R = H or OMe; R′ = CN).

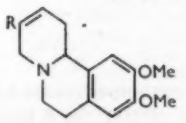
The various published syntheses[1] of the emetine skeleton (I) have involved the simultaneous or successive cyclisation of the isoquinoline and benzoquinolizine portions by the Bischler–Napieralski procedure. An alternative approach, which might offer advantages, would be by the direct linkage of an isoquinoline derivative with a suitable benzoquinolizine. Such a linkage might be achieved, for example, by Michael addition of a substituted 3,4-dihydro-1-methylisoquinoline (II) to a benzoquinolizine (III): moreover, if successful, this procedure should give a preponderance of the desired 2,3-*trans*-isomer.[1e]



(I)



(II)



(III; R = Ac or CN)

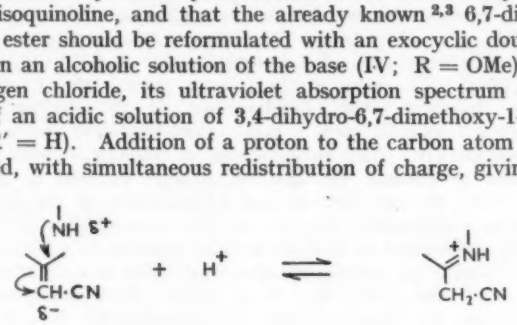
Accordingly, we have examined the possibility of using a derivative of 3,4-dihydro-1-methylisoquinoline as the reactive-methylene component of a Michael reaction with, in the first place, the highly reactive acrylonitrile. 3,4-Dihydro-6,7-dimethoxy-1-methylisoquinoline itself did not appear to react with acrylonitrile even in the presence of sodium ethoxide, and so the use of a more highly activated compound such as 1-cyanomethyl-3,4-dihydroisoquinoline (II; R = H, R′ = CN) seemed desirable.

Cyclisation of *N*-phenethyl-α-cyanoacetamide with phosphoric oxide gave a product of the expected composition, but ultraviolet (see Table) and infrared spectroscopy indicate

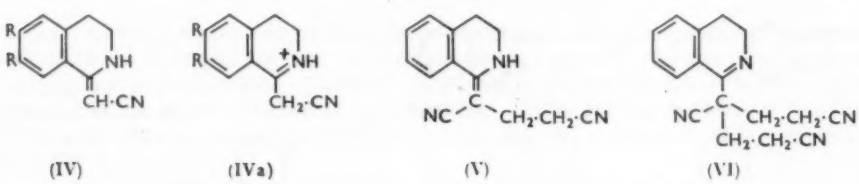
* Part II, *J.*, 1953, 2463.

[1] (*a*) Evstigneeva and Preobrazhensky, *Tetrahedron*, 1958, **4**, 223 and references cited therein; (*b*) Battersby and Openshaw, *Experientia*, 1950, **6**, 387; (*c*) Ban, *Pharm. Bull.* (*Japan*), 1955, **3**, 53; (*d*) Barash, Osbond, and Wickens, *J.*, 1959, 3530; (*e*) Battersby and Turner, *J.*, 1960, 717; (*f*) Brossi, Baumann, and Schnider, *Helv. Chim. Acta*, 1959, **42**, 1515; (*g*) Grüssner, Jaeger, Hellerbach, and Schnider, *ibid.*, 1959, **42**, 2431.

that this should be formulated as 1-cyanomethylene-1,2,3,4-tetrahydroisoquinoline (IV; R = H) rather than as 1-cyanomethyl-3,4-dihydroisoquinoline. It has characteristic absorption at 3332 and 3355 (N–H), and 2185 cm.$^{-1}$ (C≡N, conjugated) and in ethanol or acrylonitrile it has a strong absorption band at 328 mμ, whereas only a weak band at *ca.* 280 mμ (cf. 3,4-dihydro-1-methylisoquinoline) would be expected from the hypothetical 1-cyanomethyl-3,4-dihydroisoquinoline. Similarly, the spectroscopic results indicate that the ester obtained by alcoholysis of this nitrile is 1-ethoxycarbonylmethylene-1,2,3,4-tetrahydroisoquinoline, and that the already known [2,3] 6,7-dimethoxy-analogues of the nitrile and ester should be reformulated with an exocyclic double bond (*e.g.*, IV; R = OMe). When an alcoholic solution of the base (IV; R = OMe) is made 0·1N with respect to hydrogen chloride, its ultraviolet absorption spectrum changes, becoming similar to that of an acidic solution of 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (II; R = OMe, R′ = H). Addition of a proton to the carbon atom bearing the cyano-group has occurred, with simultaneous redistribution of charge, giving the cation (IVa;



R = OMe). In contrast, the base (IV; R = H) has substantially the same spectrum in 0·1N-ethanolic hydrogen chloride as in ethanol, and is thus a weaker base than its dimethoxy-analogue; in N-ethanolic hydrogen chloride, however, the ion (IVa; R = H) is formed. The cyanomethylene compound (IV; R = H) is also a weaker base than 1-ethoxycarbonylmethylene-1,2,3,4-tetrahydroisoquinoline which forms the cation (IVa; R = H; CO_2Et for CN) in 0·1N-ethanolic hydrogen chloride. This is perhaps not unexpected, for the ethoxycarbonyl group has a weaker $-I$ effect than a cyano-group, and the adjacent carbon atom is consequently more basic.



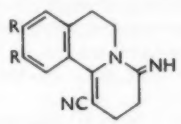
(IV) (IVa) (V) (VI)

Heating 1-cyanomethylene-1,2,3,4-tetrahydroisoquinoline (IV; R = H) with an excess of acrylonitrile at 100° for 6 hours gave a mono(cyanoethyl) compound, whilst prolonged heating gave also a di(cyanoethyl) compound. The latter is formulated as (VI), for it has no infrared absorption bands attributable to N–H or conjugated C≡N groups, and its ultraviolet spectrum is similar to that of a 1-alkyl-3,4-dihydroisoquinoline. Since the mono(cyanoethyl) compound gives the bis-product (VI) when heated with acrylonitrile, it follows that its cyanoethyl group is also located on the 1-substituent, and not on the ring nitrogen. The mono(cyanoethyl) compound, however, absorbs at 3325 (N–H), 2248 (C≡N, non-conjugated), and 2177 cm.$^{-1}$ (C≡N, conjugated), and its ultraviolet spectrum resembles that of the cyanomethylene compound (IV; R = H). The structure of the mono(cyanoethyl) compound is therefore (V).

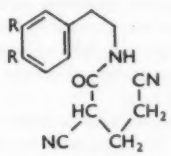
When the mono(cyanoethyl) compound (V) was treated with alcoholic sodium ethoxide at room temperature, or heated with toluene-*p*-sulphonic acid in toluene under reflux,

[2] Child and Pyman, *J.*, 1931, 36.
[3] Osbond, *J.*, 1951, 3464.

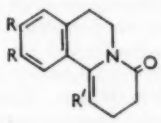
cyclisation occurred with formation of the amidine (VII; R = H). This product also resulted when the di(cyanoethyl) compound (VI) was heated with alcoholic sodium ethoxide, and, in good yield, on direct condensation of 1-cyanomethylene-1,2,3,4-tetrahydroisoquinoline (IV; R = H) with acrylonitrile in alcoholic sodium ethoxide. The structure given for the amidine is supported by light-absorption data, and was confirmed by an alternative synthesis. α-Ethoxycarbonylglutaronitrile was condensed with phenethylamine, and the resulting amide (VIII; R = H) was heated with phosphoric oxide in boiling toluene; cyclodehydration and further ring-closure occurred, yielding the amidine (VII; R = H). Replacement of phenethylamine by its 3,4-dimethoxy-derivative in this reaction sequence gave the corresponding product (VII; R = OMe), which was also obtained in excellent yield when 1-cyanomethylene-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (IV; R = OMe) was condensed with acrylonitrile in alcoholic sodium ethoxide. On being heated with aqueous mineral acid or aqueous acetic acid, the amidines (VII; R = H or OMe) were hydrolysed to the lactams (IX; R = H or OMe, R′ = CN).



(VII)



(VIII)



(IX)

Addition of acrylonitrile in alcoholic sodium ethoxide to 1-ethoxycarbonylmethylene-1,2,3,4-tetrahydroisoquinoline occurred less readily than to the 1-cyanomethylene derivative (IV; R = H). The analogous ethoxycarbonylamidine was obtained, however, as a gum which was converted, by hydrolysis, into a crystalline lactam (IX; R = H, R′ = CO_2Et).

When acrylonitrile was replaced by 1-cyanocyclohexene in the above reactions, no condensation occurred. It therefore seemed unlikely that a compound of structure (III) would react, and work along these lines was not pursued further.

Ultraviolet absorption spectra.

Compound	Solvent	$\lambda_{max.}$ (mμ)	ε
(IV; R = H)	EtOH	247, 328	14,300, 11,300
	Acrylonitrile	248, 329	14,500, 10,800
	0·1N-HCl–EtOH	248, 326	12,300, 10,000
	N-HCl–EtOH	285, 321 *	11,500, 3550
(IV; R = H; CO_2Et for CN)	EtOH	248, 335	14,200, 14,400
	0·1N-HCl–EtOH	281, 317 *	13,100, 2670
(II; R = R′ = H)	EtOH	250, 280 *	8800, 1460
	0·1N-HCl–EtOH	272, 310 *	11,900, 1800
(IV; R = OMe)	EtOH	227, 272, 320	23,300, 10,300, 17,300
	0·1N-HCl–EtOH	216, 250, 315, 365	10,800, 15,100, 10,700, 8900
(IV; R = OMe; CO_2Et for CN)	EtOH	227, 268,* 273, 331	23,100, 8400, 8740, 20,800
	0·1N-HCl–EtOH	247, 309, 362	17,200, 9550, 9430
(II; R = OMe, R′ = H)	EtOH	227, 272, 308	23,600, 7570, 6660
	0·1N-HCl–EtOH	245, 303, 354	18,400, 9300, 8910
(V)	EtOH / 0·1N-HCl–EtOH	234, 245, 325	11,650, 10,900, 10,500
	Acrylonitrile	243, 326	11,800, 12,300
(VI)	EtOH	253, 284	8300, 1600
(VII; R = H)	0·1N-NaOH–EtOH	249, 320	14,250, 10,900
(VII; R = OMe)	0·1N-NaOH–EtOH	236, 249,* 282, 317	18,300, 14,300, 10,500, 16,300
(IX; R = H, R′ = CN)	EtOH	244, 308	13,400, 9900
(IX; R = OMe, R′ = CN)	EtOH	215, 225, 240, 280, 329	17,500, 16,600, 18,300, 9390, 13,800
(IX; R = H, R′ = CO_2Et)	EtOH	235, 302	13,800, 8670

* Inflexion.

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Experimental

Ultraviolet spectra were determined with a Hilger Uvispek instrument. Infrared spectra were measured for potassium chloride dispersions, by means of a Unicam S.P. 100 spectrophotometer with grating accessory, at a computed spectral slit width of *ca.* 3 cm.$^{-1}$. Solids were dried *in vacuo* over silica gel.

1-*Cyanomethylene*-1,2,3,4-*tetrahydroisoquinoline* (IV; R = H).—A solution of *N*-phenethyl-α-cyanoacetamide [4] (70 g.) in hot toluene (1260 ml.) was heated until 70 ml. of toluene had distilled. The solution was refluxed and, with occasional shaking, treated with portions of phosphoric oxide (140, 140, and 95 g.) at intervals of 30 min. After a further 30 min., the mixture was cooled, decomposed with ice-water (1500 ml.), and stirred, with cooling, until all the solid had dissolved (*ca.* 3 hr.). The liquid was filtered (Hyflo), the aqueous layer separated, and the toluene layer extracted with 2N-hydrochloric acid (2 × 350 ml.). The combined aqueous solution was washed with ether (2 × 500 ml.), and agitated with a vigorous current of nitrogen to remove traces of ether. The solution was basified with concentrated aqueous potassium hydroxide, with cooling, and the precipitated solid was collected, washed with water, and dried. The yellow solid (33 g.) was digested with hot light petroleum (b. p. 80—100°) (2800 ml.), and the petroleum solution was decanted from a dark residue, reheated, decolorised (activated charcoal), and set aside, giving pale yellow prisms (24·6 g.), m. p. 98·5—99°, of 1-*cyanomethylene*-1,2,3,4-*tetrahydroisoquinoline* (Found: C, 78·0; H, 6·1; N, 16·4. $C_{11}H_{10}N_2$ requires C, 77·6; H, 5·9; N, 16·45%).

Reaction of 1-*Cyanomethylene*-1,2,3,4-*tetrahydroisoquinoline* (IV; R = H) *with Acrylonitrile*.—(*a*) A mixture of the base (IV; R = H) (2 g.) and acrylonitrile (1·24 g., 2 mol.) was heated in a sealed tube at 100° for 6 hr. Crystals separated from the cooled liquid. The mixture was digested with warm ether (25 ml.) and cooled to 0°, and the crystals (1·88 g.), m. p. 135—137°, were collected. Recrystallisation from methanol afforded colourless flat needles (1·58 g.) of 1-(1,3-*dicyanopropylidene*)-1,2,3,4-*tetrahydroisoquinoline* (V), m. p. 137—138° (Found: C, 75·75; H, 5·75; N, 18·5. $C_{14}H_{13}N_3$ requires C, 75·3; H, 5·85; N, 18·8%). From the ethereal liquors some unchanged starting material was isolated.

(*b*) When the base (IV; R = H) (20 g.) and acrylonitrile (18·6 g., 3 mol.) were heated together under reflux for 30 hr., the temperature of the solution increased from 83° to 93°. After cooling, the mass of crystals was taken up in hot benzene (300 ml.), 100 ml. of solvent were distilled, and the residual solution was set aside to give colourless crystals of the product (V) (16·88 g.), m. p. 136·5—138°. The benzene liquors were evaporated *in vacuo* and a solution of the residual gum in methanol was evaporated. The residual gum was dissolved in hot methanol (20 ml.) and set aside, giving crystals (9·4 g.) of m. p. 92—99° [m. p. 80—95° in admixture with (IV; R = H)]. These, recrystallised from methanol, afforded colourless prisms (8·56 g.), m. p. 98—99·5°, of 1-(1,3-*dicyano*-1-2′-*cyanoethylpropyl*)-3,4-*dihydroisoquinoline* (VI) (Found: C, 73·8; H, 5·75; N, 20·6. $C_{17}H_{16}N_4$ requires C, 73·9; H, 5·85; N, 20·3%). The di(cyanoethyl) compound (VI) (0·25 g.), m. p. 97—98·5°, and unchanged compound (V) (0·44 g.), m. p. 133—135°, also resulted from heating a mixture of the mono-derivative (V) (1 g.) and acrylonitrile (0·48 g., 2 mol.) in a sealed tube at 100° for 9 hr.

1-*Cyano*-3,4,6,7-*tetrahydro*-4-*imino*-2H-*benzo*[a]*quinolizine* (VII; R = H).—(*a*) A solution of the mono(cyanoethyl) compound (V) (9·3 g.) in hot ethanol (180 ml.) was cooled quickly, and the resulting suspension of fine crystals was added to a solution of sodium (9·3 g.) in ethanol (270 ml.). The crystals dissolved immediately, and soon the product began to crystallise. After 1 hr. at room temperature, the alcohol was evaporated *in vacuo*, and the residual solid was shaken with ice-cold water (450 ml.) and benzene (450 ml.). The benzene solution was separated, washed with water, and then extracted with 0·25N-acetic acid (2 × 400 ml.). The combined extract was gradually basified with aqueous potassium hydroxide, with seeding, and the resulting crystals were collected and washed with water. The dried product (8·9 g.), m. p. 146—147°, crystallised from alcohol (50 ml.), yielding colourless flat needles (7·77 g.) of pure *amidine* (VII; R = H) which began to melt at 140°, then resolidified, with m. p. 147—148° (Found: C, 75·6; H, 5·65; N, 18·85. $C_{14}H_{13}N_3$ requires C, 75·3; H, 5·85; N, 18·8%), $\nu_{max.}$ 2190 (C≡N, conjugated), 3299 cm.$^{-1}$ (N–H).

(*b*) A solution of toluene-*p*-sulphonic acid (0·85 g.) in hot toluene (25 ml.) was distilled until 5 ml. of liquid had been collected, and the residual anhydrous solution was heated with

[4] Leonard and Boyer, *J. Amer. Chem. Soc.*, 1950, **72**, 2980.

the mono(cyanoethyl) compound (V) (1 g.) under reflux for 1 hr. At first an oil was formed, but this soon gave place to crystals of the toluene-*p*-sulphonate of the amidine (VII; R = H). The cooled mixture was shaken with water (25 ml.), and the crystals were collected (solid A). The aqueous filtrate was separated from the toluene layer, washed once with toluene, then basified with aqueous potassium hydroxide, and the precipitated solid was collected (solid B). A stirred suspension of solid A in water (200 ml.) was basified with potassium hydroxide, and the resulting base was collected, combined with solid B, and shaken with water (60 ml.) containing just more than the equivalent amount of glacial acetic acid. The resulting solution was filtered from a brown sediment and basified with potassium hydroxide, with seeding, giving crystals of the amidine (VII; R = H) (0·74 g.), which began to melt at 140°, then resolidified, with m. p. 147—148°.

(*c*) The amidine (VII; R = H) (0·42 g.) resulted when the di(cyanoethyl) compound (VI) (1 g.) was heated with a solution of sodium (1 g.) in anhydrous ethanol (25 ml.) under reflux for 30 min.

(*d*) A stirred solution of sodium (0·54 g.) in ethanol (30 ml.) was treated with the isoquinoline compound (IV; R = H) (4 g.) and acrylonitrile (1·38 g.), and kept at 50—60° under nitrogen for 2 hr. The cooled product was worked up in the manner of (*a*), giving the amidine (VII; R = H) (4·18 g.) of the same m. p.

(*e*) An equimolecular mixture of phenethylamine (14·6 g.) with α-ethoxycarbonylglutaronitrile [5] (20 g.) was heated rapidly to 126° (alcohol then began to distil) and then during 30 min. to 180°. The residual crude amide (VIII; R = H) (29·4 g.) was cooled slightly and dissolved in toluene (530 ml.), and the solution was heated until 30 ml. of liquid had distilled. The toluene solution was heated under reflux and treated with phosphoric oxide (59 g., 59 g., and 40 g.), and the product was isolated in the manner described for the preparation of base (IV; R = H). The crude orange-brown base (5·4 g.) was twice crystallised from acetone, giving colourless prisms (1·73 g.) of the amidine (VII; R = H) which began to melt at 140°, then resolidified, with m. p. 147—148°. Recrystallisation from alcohol afforded flat needles of the same m. p., alone and in admixture with amidine obtained by method (*a*) (Found: C, 75·3; H, 5·85; N, 18·9%).

1-*Cyanomethylene*-1,2,3,4-*tetrahydro*-6,7-*dimethoxyisoquinoline* (IV; R = MeO).—Cyclisation of *N*-(3,4-dimethoxyphenethyl)-α-cyanoacetamide by Osbond's method [3] gave the isoquinoline (IV; R = MeO) as needles, m. p. 170—171°, $\nu_{max.}$ 2182 (C≡N, conjugated) and 3339 cm.$^{-1}$ (N–H).

1-*Cyano*-3,4,6,7-*tetrahydro*-4-*imino*-9,10-*dimethoxy*-2H-*benzo*[a]*quinolizine* (VII; R = MeO).—(*a*) A solution of sodium (1 g.) in ethanol (60 ml.) was treated with the isoquinoline compound [3] (IV; R = MeO) (10 g.), and then with acrylonitrile (2·54 g.). The mixture was heated under nitrogen on the steam-bath for 30 min., then cooled, and the resulting crystals were collected and washed with alcohol, giving 10·27 g., m. p. 156—158°, of the amidine (VII; R = MeO). The alcoholic liquors were evaporated, the residual solid was shaken with water (200 ml.) and benzene (200 ml.), and the benzene solution was washed with water, then extracted with water (200 ml.) containing glacial acetic acid (3 ml.). The acid extract was basified with aqueous potassium hydroxide, with seeding, giving pale yellow crystals (1·55 g.), m. p. 156—157·5°, of less pure amidine. The major product, recrystallised from alcohol (60 ml.), gave colourless prisms (8·72 g.), m. p. 158—159°, of pure *amidine* (VII; R = MeO) (Found: C, 67·95; H, 5·95; N, 14·65. $C_{16}H_{17}N_3O_2$ requires C, 67·8; H, 6·05; N, 14·85%).

(*b*) An equimolecular mixture of 3,4-dimethoxyphenethylamine (16·4 g.) with α-ethoxycarbonylglutaronitrile [5] (15 g.) was heated quickly to 120°, and then during 30 min. to 180°. The residual crude amide (VIII; R = MeO) was heated *in vacuo* on the steam-bath, to remove traces of alcohol, and dissolved in hot toluene (250 ml.). The toluene solution was heated until 10 ml. of liquid had distilled and treated under reflux with three 30 g. portions of phosphoric oxide at intervals of 30 min. After a further 30 minutes' refluxing, the mixture was cooled, stirred with ice, and kept at an alkaline pH by periodical addition of strong aqueous sodium hydroxide, with external cooling in ice-water. When, after *ca.* 3 hr., all lumps had disintegrated, the liquid was filtered (Hyflo), and the insoluble residue was washed with water and toluene. The toluene layer was separated, washed with water, and extracted with a solution of glacial acetic acid (10 ml.) in water (200 ml.). Basification of the extract with sodium hydroxide gave a thick oil which soon solidified, and the solid was collected, pulverised, and then washed with water. The dried solid (7·31 g.) crystallised from alcohol (35 ml.) as pale yellow-brown

[5] Rogers, U.S.P. 2,460,536/1949.

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prisms (5·2 g.), m. p. 158—159°, of almost pure amidine (VII; R = MeO). It did not prove possible to remove completely the trace of coloured impurity present in these prisms. A lukewarm solution in benzene (400 ml.) was treated with a little activated alumina, filtered, and extracted with a solution of glacial acetic acid (4 ml.) in water (300 ml.). The extract was basified with sodium hydroxide, giving a pale yellow solid which crystallised from alcohol as pale yellow prisms, almost colourless when powdered, of m. p. 158—159°, alone and in admixture with the amidine obtained by method (*a*).

1-*Cyano*-3,4,6,7-*tetrahydro*-4-*oxo*-2H-*benzo*[a]*quinolizine* (IX; R = H, R′ = CN).—When a solution of the amidine (VII; R = H) (0·52 g.) in water (10 ml.) containing glacial acetic acid (1 ml.) was heated on the steam-bath, colourless plates soon began to separate. After 30 minutes' heating, the suspension was cooled, diluted with water, and filtered, yielding 0·49 g. of the *lactam* (IX; R = H, R′ = CN), which almost completely melted at 146—147°, then resolidified, with m. p. 149—150°. The aqueous filtrate liberated ammonia on being heated with potassium hydroxide. The *lactam* depressed the m. p. of the starting material and crystallised from light petroleum (b. p. 80—100°) in colourless long flat needles of the above m. p. (Found: C, 74·75; H, 5·15; N, 12·55; O, 7·40. $C_{14}H_{12}N_2O$ requires C, 75·0; H, 5·4; N, 12·5; O, 7·15%), $\nu_{max.}$ 1674 (C=O), 2198 cm.$^{-1}$ (C≡N, conjugated). The lactam (IX; R = H, R′ = CN) was also produced when a solution of the amidine (VII; R = H) in dilute aqueous hydrochloric acid was heated on the steam-bath.

1-*Cyano*-3,4,6,7-*tetrahydro*-9,10-*dimethoxy*-4-*oxo*-2H-*benzo*[a]*quinolizine* (IX; R = MeO, R′ = CN).—A solution of the amidine (VII; R = MeO) (1·16 g.) in water (20 ml.) containing glacial acetic acid (2 ml.) was heated on the steam-bath for 1 hr., yielding the *lactam* (IX; R = MeO, R′ = CN) (1·14 g.), m. p. 146—147·5°. Recrystallisation from alcohol afforded colourless prisms, m. p. 146·5—147·5° (Found: C, 67·75; H, 5·5; N, 9·95. $C_{16}H_{16}N_2O_3$ requires C, 67·6; H, 5·65; N, 9·85%).

1-*Ethoxycarbonylmethylene*-1,2,3,4-*tetrahydroisoquinoline* (IV; R = H; CO_2Et for CN) was prepared from the cyanomethylene compound (IV; R = H) in the manner described by Osbond [3] for the alcoholysis of base (IV; R = MeO). On distillation, the ester was obtained as a pale yellow oil, b. p. 140°/0·08 mm. (Found: C, 72·05; H, 7·0; N, 6·75. $C_{13}H_{15}NO_2$ requires C, 71·85; H, 6·95; N, 6·45%).

1-*Ethoxycarbonyl*-3,4,6,7-*tetrahydro*-4-*oxo*-2H-*benzo*[a]*quinolizine* (IX; R = H, R′ = CO_2Et).—A solution of sodium (0·21 g.) in dry ethanol (6 ml.) was treated with 1-ethoxycarbonylmethylene-1,2,3,4-tetrahydroisoquinoline (2 g.) and acrylonitrile (0·74 g.) and set aside at room temperature for 17 hr. The alcohol was evaporated *in vacuo*, the residue was shaken with benzene and water, and the benzene layer was washed with water and extracted with dilute aqueous acetic acid. The extract was basified with potassium hydroxide, giving an oil, which was taken up in ether. The ethereal solution was washed with water and evaporated, and the residual gum was heated with water (15 ml.) and glacial acetic acid (1 ml.) on the steam-bath for 30 min. The resulting crystals (0·14 g.), m. p. 123—125°, recrystallised from light petroleum (b. p. 80—100°), giving colourless prisms of the *lactam* (IX; R = H, R′ = CO_2Et), m. p. 124·5—125·5° (Found: C, 71·1; H, 6·25; N, 5·3. $C_{16}H_{17}NO_3$ requires C, 70·85; H, 6·3; N, 5·15%).

1-*Ethoxycarbonylmethylene*-1,2,3,4-*tetrahydro*-6,7-*dimethoxyisoquinoline* (IV; R = MeO; CO_2Et for CN).—Alcoholysis of base (IV; R = MeO) by Osbond's method,[3] and crystallisation of the product from light petroleum (b. p. 60—80°), and then from alcohol, gave colourless prisms of the ester (IV; R = MeO; CO_2Et for CN), m. p. 86—87°, $\nu_{max.}$ 1651 (C=O) and 3305 cm.$^{-1}$ (N–H). Infrared absorption maxima for a 0·01M-solution in carbon tetrachloride were the same. The C=O stretching frequency is *ca.* 60 cm.$^{-1}$ lower than that of a simple αβ-unsaturated ester, suggesting a resonance-stabilised interaction of the carbonyl-oxygen and the amino-hydrogen atom.

We are grateful to Dr. A. J. Everett for the light-absorption measurements and for helpful discussion of the results, to Mr. P. R. W. Baker for the microanalyses, and to Mr. J. M. Raymond for technical assistance.

The Wellcome Research Laboratories, Beckenham, Kent. [*Received, June 14th*, 1961.]

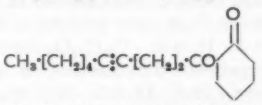
974. *Synthesis of* (±)-cis-9-*Hydroxyoctadec*-12-*enoic Acid.*

By J. Kennedy, A. Lewis, N. J. McCorkindale, and R. A. Raphael.

The structure assigned to a naturally-occurring isomer of ricinoleic acid has been confirmed by synthesis of the racemate.

The lævorotatory isomer of ricinoleic acid occurring in the seed oil of *Strophanthus sarmentosus*,[1] *S. hispidus, and S. courmontii* [2] has been shown by degradative studies [1] to be *cis*-9-hydroxyoctadec-12-enoic acid (I). Synthetic confirmation of this constitution has been obtained in the following manner.

$$CH_3\cdot[CH_2]_4\cdot CH{:}CH\cdot[CH_2]_2\cdot CH(OH)\cdot[CH_2]_7\cdot CO_2H \quad (I)$$



(II)

$$CH_3\cdot[CH_2]_4\cdot C{\equiv}C\cdot[CH_2]_2\cdot CO\cdot[CH_2]_n\cdot CO_2H \quad (III)$$

Oct-2-yn-1-ol was conveniently prepared by alkylation of tetrahydropyranyloxyprop-1-yne with n-pentyl bromide and subsequent acid hydrolysis. Malonation of the corresponding bromide followed by hydrolysis and decarboxylation gave crystalline dec-4-ynoic acid. The acid chloride of the latter was condensed with 1-morpholinocyclohex-1-ene to produce, after hydrolysis, 2-dec-4′-ynoylcyclohexan-1-one (II); basic hydrolysis of this β-diketone gave 7-oxohexadec-10-ynoic acid (III; $n = 5$), chain extension of which was carried out by the following sequence. Simultaneous acid-catalysed ketalisation and esterification were effected with an excess of ethylene glycol, and the product was reduced with lithium aluminium hydride to give, after acid hydrolysis, 7-oxohexadec-10-yn-1-ol. Malonation of the derived bromide, hydrolysis, and decarboxylation furnished 9-oxo-octadec-12-ynoic acid (III; $n = 7$). An attempt was made to obtain this acid more simply by treating 1-morpholinocyclo-oct-1-ene with dec-4-ynoyl chloride followed by basic fission of the resulting 2-dec-4′-ynoylcyclo-octan-1-one. Unfortunately, treatment of the latter β-diketone with a wide variety of basic reagents produced fission in the unwanted manner with regeneration of cyclo-octanone and dec-4-ynoic acid.

Reduction of 9-oxo-octadec-12-ynoic acid, first with sodium borohydride and then with hydrogen in the presence of Lindlar catalyst, gave the required *cis*-9-hydroxyoctadec-12-enoic acid. This synthetic racemate was identical in all physical properties, except optical rotation, with the naturally-occurring lævorotatory acid kindly provided by Dr. F. D. Gunstone. For a more direct comparison, the latter acid was converted into the racemate by oxidation to the crystalline *cis*-9-oxo-octadec-12-enoic acid and reduction of this keto-acid with sodium borohydride.

Experimental

Oct-2-yn-1-ol.—Tetrahydropyranyloxyprop-1-yne [3] (35 g.) in ether (50 ml.) was added during 1 hr. to a stirred suspension of sodamide in liquid ammonia, prepared from sodium (6·5 g.). After 2 hr., n-pentyl bromide (41·0 g.) in ether (50 ml.) was added dropwise over 1 hr. The mixture was stirred for a further 4 hr., and the ammonia was allowed to evaporate overnight. The product obtained after addition of water and isolation by ether extraction, was dissolved in methanol (125 ml.) containing 25% aqueous sulphuric acid (10 ml.) and left for 8 hr. at room temperature. The mixture was poured into water (250 ml.), the solution was extracted with ether, and the ether extracts were washed successively with aqueous sodium hydrogen carbonate and sodium chloride. Distillation gave oct-2-yn-1-ol (39·4 g., 63%), b. p. 102—106°/23 mm., n_D^{25} 1·4540 (lit.,[4] b. p. 76—82°/2 mm., n_D^{20} 1·4550).

Diethyl Oct-2-ynylmalonate.—A stirred solution of diethyl sodiomalonate, prepared from

[1] Gunstone, *J.*, 1952, 1274.
[2] Gunstone, *J. Sci. Food Agric.*, 1953, **4**, 129.
[3] Henbest, Jones, and Walls, *J.*, 1950, 3646.
[4] Taylor and Strong, *J. Amer. Chem. Soc.*, 1950, **72**, 4263.

XUM

diethyl malonate (197 g.), sodium (22·7 g.), and ethanol (1100 ml.), was treated dropwise with 1-bromo-oct-2-yne [4] (143 g.), and the mixture was refluxed for 6 hr. After concentration of the ethanol solution, water (500 ml.) was added and the mixture extracted with ether. Distillation gave *diethyl oct-2-ynylmalonate* (145 g., 71%), b. p. 124—128°/0·3 mm., $n_D^{17.5}$ 1·4488 (Found: C, 67·1; H, 8·85. $C_{15}H_{24}O_4$ requires C, 67·1; H, 9·0%). There was also obtained a higher-boiling fraction consisting of *diethyl dioct-2-ynylmalonate* (25 g., 9%), b. p. 154—160°/0·3 mm., n_D^{25} 1·4620 (Found: C, 73·0; H, 9·5. $C_{23}H_{36}O_4$ requires C, 73·4; H, 9·6%).

Oct-2-ynylmalonic Acid.—Diethyl oct-2-ynylmalonate (145 g.) was hydrolysed by refluxing it for 3 hr. with potassium hydroxide (91 g.) in ethanol (700 ml.). The *malonic acid* crystallised from light petroleum (b. p. 60—80°) as plates (93 g., 80%), m. p. 110—111° (Found: C, 62·2; H, 7·5. $C_{11}H_{16}O_4$ requires C, 62·2; H, 7·6%).

Dec-4-ynoic Acid.—Oct-2-ynylmalonic acid (47·5 g.) was heated in an oil bath at 160° for 3 hr. The product, *dec-4-ynoic acid* crystallised from light petroleum (b. p. 40—60°) as plates (27 g., 72%), m. p. 36·5—37° (Found: C, 71·5; H, 9·3. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). The *anilide* crystallised from benzene–light petroleum as needles, m. p. 105—105·5° (Found: C, 79·1; H, 8·4; N, 5·7. $C_{16}H_{21}NO$ requires C, 79·0; H, 8·7; N, 5·8%).

Hydrogenation in ethanol over 10% palladium–charcoal and crystallisation from light petroleum (b. p. 40—60°) gave decanoic acid, m. p. 30—31° (lit., m. p. 31°) (Found: C, 69·6; H, 11·4. Calc. for $C_{10}H_{20}O_2$: C, 69·7; H, 11·7%) [anilide, m. p. 69°, from benzene–light petroleum (lit., m. p. 69·5°) (Found: C, 77·5; H, 10·1; N, 5·7. Calc. for $C_{16}H_{25}NO$: C, 77·7; H, 10·2; N, 5·7%)].

Dec-4-ynoyl Chloride.—A solution of dec-4-ynoic acid (58 g.) in benzene (120 ml.) was treated dropwise with oxalyl chloride (52 g.) and the mixture was left at room temperature overnight. Distillation gave the acid chloride as an oil (57 g., 90%), b. p. 76—78°/0·5 mm., n_D^{26} 1·4592, $\nu_{max.}$ (thin film) 1800 cm.$^{-1}$.

2-Dec-4′-ynoylcyclohexanone.—Dec-4-ynoyl chloride (23 g.) in dry chloroform (50 ml.) was added slowly to a solution of 1-morpholinocyclohex-1-ene [5] (23 g.) and triethylamine (15·2 g.) in dry chloroform (50 ml.) at 40°. After a further 1 hr. at 40°, the mixture was stirred overnight at room temperature; 20% sulphuric acid (95 ml.) was added and the mixture was refluxed for 6 hr. The chloroform layer was separated and washed with water until the washings were at pH 6. The combined aqueous layer and washings were brought to pH 6 with 2N-aqueous sodium hydroxide and extracted with chloroform. Distillation of the combined chloroform extracts gave *2-dec-4′-ynoylcyclohexanone* (19 g., 62%), b. p. 130°/10^{-3} mm., n_D^{25} 1·5032 (Found: C, 77·3; H, 9·85. $C_{16}H_{24}O_2$ requires C, 77·3; H, 9·75%); $\nu_{max.}$ (thin film) 3200—2700, 1600 cm.$^{-1}$; $\lambda_{max.}$ (ethanol) 290 mμ (ε 8090).

7-Oxohexadec-10-ynoic Acid.—2-Dec-4′-ynoylcyclohexanone (18 g.) was refluxed with 10% aqueous potassium hydroxide (75 ml.) for 3 hr., and set aside overnight. Acidification with 3N-sulphuric acid and ether extraction gave the *acid*, which crystallised from aqueous ethanol as plates (15 g., 79%), m. p. 57·5—58° (Found: C, 72·35; H, 9·7. $C_{16}H_{26}O_3$ requires C, 72·15; H, 9·8%); $\nu_{max.}$ (Nujol mull) 1705, 1700 cm.$^{-1}$. The *anilide* crystallised from aqueous ethanol as needles, m. p. 107—108° (Found: C, 76·7; H, 9·2; N, 4·4. $C_{22}H_{31}NO_2$ requires C, 77·3; H, 9·15; N, 4·1%).

2-Dec-4′-ynoylcyclo-octanone. Cyclo-octanone (12·6 g.), morpholine (8·7 g.) and toluene-*p*-sulphonic acid (0·2 g.) were refluxed in benzene (40 ml.) until water no longer separated (*ca.* 4 hr.). The cooled mixture was washed with saturated aqueous sodium hydrogen carbonate and dried. Distillation gave 1-morpholinocyclo-oct-1-ene (19·5 g., 70%), b. p. 142—148°/12 mm., n_D^{21} 1·5148.

Acylation of the above enamine with dec-4-ynoyl chloride (3·73 g.) as in the above cognate preparation gave *2-dec-4′-ynoylcyclo-octan-1-one* as an oil (2·1 g., 38%), b. p. 150—156°/0·1 mm., n_D^{21} 1·5050 (Found: C, 78·0; H, 10·3. $C_{18}H_{28}O_2$ requires C, 78·2; H, 10·2%); $\nu_{max.}$ (thin film) 3200—2700, 1600 cm.$^{-1}$; $\lambda_{max.}$ (ethanol) 290 mμ (ε 6700).

Treatment of this β-diketone with alkali under the conditions described above for the analogous cyclohexanone, gave, as the only products, dec-4-ynoic acid (76%), subliming at 60°/10^{-4} mm., m. p. and mixed m. p. 35°, together with cyclo-octanone (67%) [2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 174°]. Similar results were obtained when the diketone was refluxed for 30 hr. with aqueous barium hydroxide or kept for 12 hr. in dilute aqueous alcoholic potassium hydroxide.

[5] Hunig, Benzing, and Lucke, *Chem. Ber.*, 1957, **90**, 2833.

7-*Oxohexadec*-10-*yn*-1-*ol*.—7-Oxohexadec-10-ynoic acid (28 g.), ethylene glycol (12 g.), and toluene-*p*-sulphonic acid (0·3 g.) were refluxed in benzene (400 ml.), with constant separation of water, for 36 hr. The cooled mixture was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated to give the crude ketal-ester (33 g.), $\nu_{max.}$ (thin film) 3500, 1745, 1070 cm.$^{-1}$.

This ketal-ester in ether (60 ml.) was slowly added dropwise to a stirred slurry of lithium aluminium hydride (7·4 g.) in ether (100 ml.), and the mixture was refluxed for 12 hr. After destruction of the excess of hydride with ethyl acetate, water (100 ml.) was added and the mixture was extracted with ether. Evaporation gave the ketal, $\nu_{max.}$ (thin film) 3400, 1080 cm.$^{-1}$.

The crude ketal, in ether (75 ml.), was shaken with 6N-sulphuric acid (80 ml.) for 6 hr. The ether layer was washed with saturated aqueous sodium hydrogen carbonate and dried. Evaporation gave the *alcohol*, which crystallised from methanol as plates (17·3 g., 65%), m. p. 41—42° (Found: C, 76·0; H, 10·9. $C_{16}H_{28}O_2$ requires C, 76·1; H, 11·2%); $\nu_{max.}$ (Nujol mull) 3350, 1705 cm.$^{-1}$.

Diethyl 7-*Oxohexadec*-10-*ynylmalonate*.—Phosphorus tribromide (1·26 g.) was added dropwise to a cooled solution of 7-oxohexadec-10-yn-1-ol (3·51 g.) and pyridine (5 ml.) in ether (20 ml.). After a 4 hours' reflux, water (20 ml.) was added and the mixture was extracted with ether. The ether extracts were washed successively with 25% sulphuric acid, saturated aqueous sodium hydrogen carbonate, and brine. Evaporation gave crude 1-bromo-7-oxohexadec-10-yne (3·2 g.), $\nu_{max.}$ (thin film) 1705 cm.$^{-1}$.

The crude bromo-compound was added dropwise to a solution prepared from sodium (0·46 g.), ethanol (15 ml.), and diethyl malonate (2·4 g.). After 5 hours' reflux, the solution was concentrated to half its volume and water (15 ml.) was added. Ether extraction afforded *diethyl* 7-*oxohexadec*-10-*ynylmalonate* (1·86 g., 46%), b. p. 138—146°/10^{-3} mm. (Found: C, 69·6; H, 9·4. $C_{23}H_{38}O_5$ requires C, 70·0; H, 9·7%); $\nu_{max.}$ (thin film) 1748, 1720 cm.$^{-1}$.

7-*Oxohexadec*-10-*ynylmalonic Acid*.—The substituted malonic ester (8·0 g.) was refluxed for 2 hr. with potassium hydroxide (2·3 g.) in aqueous ethanol (60 ml.). After removal of solvent, water (30 ml.) was added and the mixture was extracted with ether to remove unchanged ester. The aqueous solution was acidified, and extracted with ether to give the *malonic acid* which crystallised from ethyl acetate–light petroleum as plates (4·5 g., 66%), m. p. 108—109° (Found: C, 67·0; H, 8·7. $C_{19}H_{30}O_5$ requires C, 67·4; H, 8·9%).

9-*Oxo-octadec*-12-*ynoic Acid*.—7-Oxohexadec-10-ynylmalonic acid (2·5 g.) was heated at 160° (oil bath) until evolution of carbon dioxide had ceased. The product, in ether, was filtered through a short silica column. The *acid* crystallised from light petroleum (b. p. 40—60°) as plates (1·1 g., 51%), m. p. 66—67° (Found: C, 73·5; H, 10·3. $C_{18}H_{30}O_3$ requires C, 73·4; H, 10·3%); $\nu_{max.}$ (Nujol mull) 1710, 1705 cm.$^{-1}$.

(±)-cis-9-*Hydroxyoctadec*-12-*enoic Acid*.—(*i*) 9-Oxo-octadec-12-ynoic acid (200 mg.) in ethanol (3 ml.) was treated with sodium borohydride (80 mg.) in water (2 ml.) and kept at 0° for 24 hr. 4% Aqueous sodium hydroxide (1 ml.) was added and the mixture was heated on the steam bath for 1 hr. Acidification and ether extraction gave 9-hydroxyoctadec-12-ynoic acid which, after several crystallisations from light petroleum (b. p. 40—60°) at −70°, formed waxy plates (100 mg., 50%), m. p. 38—42°.

The above hydroxy-acid (40 mg.) in ethanol (10 ml.) was hydrogenated over Lindlar catalyst (30 mg.) until 1 mol. of hydrogen was absorbed. After removal of the catalyst and evaporation, crystallisation of the residue from light petroleum (b. p. 40—60°) at −70° gave (±)-*cis*-9-hydroxyoctadec-12-enoic acid as waxy plates (35 mg., 87%), m. p. 28—32°. The infrared and mass spectra were identical with those of the naturally occurring (−)-enantiomorph, m. p. 30—34°.

(*ii*) 9-Oxo-octadec-12-enoic acid [see (*i*) below] (40 mg.) was reduced with sodium borohydride in aqueous ethanol as in the above experiment. (±)-9-Hydroxyoctadec-12-enoic acid was obtained as a solid (25 mg.), m. p. 24—28°. The infrared spectrum was identical with that of the (±)-acid obtained as above.

cis-9-*Oxo-octadec*-12-*enoic Acid*.—(*i*) Natural *cis*-9-hydroxyoctadec-12-enoic acid (0·5 g.) in acetone (5 ml.) was cooled to 0°, and a solution of chromium trioxide (0·12 g.) in concentrated sulphuric acid (0·4 g.) and water (1 ml.) was added dropwise. After 6 hr., water was added and the mixture was extracted with ether. Evaporation and crystallisation from light petroleum (b. p. 40—60°) at −70° gave the *keto-acid* as plates (0·35 g., 70%), m. p. 44—45° (Found: C, 72·5; H, 10·8. $C_{18}H_{32}O_3$ requires C, 72·9; H, 10·9%); $\nu_{max.}$ (Nujol mull) 1710, 1705 cm.$^{-1}$.

(*ii*) Oxidation of synthetic (±)-*cis*-9-hydroxyoctadec-12-enoic acid (20 mg.) under the same conditions gave, after crystallisation, plates (14 mg.), m. p. 40—42°. This was shown by mixed m. p. and by the identity of the respective infrared and mass spectra to be identical with a sample of the keto-acid prepared as in (*i*).

The authors thank Mr. J. M. Cameron, B.Sc., and his assistants for microanalyses and Mr. W. K. Reid for determining the mass spectra. This work was carried out during the tenure of a Gas Council Scholarship (by J. K.), of an Aliphatic Research Company Grant (by A. L.), and of an I.C.I. Fellowship (by N. J. McC.).

THE UNIVERSITY, GLASGOW, W.2. [*Received, July 10th*, 1961.]

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975. *Electron-donor and -acceptor Complexes with Aromatic Systems. Part VII.*[1] *Electron-donor and -acceptor Complexes of Some Tetracyclic Aromatic and Hetero-aromatic Molecules.*

By G. C. MARTIN and A. R. UBBELOHDE.

Naphthacene, 1,2-benzanthracene and their aromatic aza-analogues 2,3-, 3,4-, and 1,2-benzacridine have been investigated with regard to dark-current conductivities of the pure solids at various temperatures. Similar measurements have been made on chloro- and oxo-derivatives of the benzacridines which were obtained in the preparative work. For all the parent molecules, a parallelism is found between the activation energy controlling conduction and the ultraviolet absorption band of lowest energy, $^1E_1$. On this basis, some edge substituents showed lowered activation energies for conduction in the solids.

Complexes of these tetracyclic molecules have been prepared with iodine as a typical electron acceptor, and with sodium as a typical electron donor, and have been studied in various ways. For solutions in carbon tetrachloride, absorption spectra indicate that 1 : 1 complexes with iodine are bonded differently for the homonuclear ($\pi \longrightarrow I_2$) and aza-aromatic ($^nN \longrightarrow I_2$) molecules, except in the case of 3,4-benzacridine where steric effects appear to favour ($\pi \longrightarrow I_2$) polarisation bonds. For the solids, molar volumes determined by pyknometry bear out this difference. $\pi \longrightarrow I_2$ complexes with iodine all showed higher conductivities and the activation energy for conduction was lower than for the parent molecules. $^nN \longrightarrow I_2$ complexes showed higher conductivities, but the energy gap was increased instead of lowered. Where available, measurements of thermoelectric power showed that in these solids majority charge carriers are positive.

Sodium complexes on the other hand showed no clear difference between the aromatic and the aza-aromatic molecules. For all these solids, the conductivity of the complex was condiserably increased, and the energy gap was somewhat lowered, in comparison with that of the parent molecule. Measured molar volumes suggest that polarisation bonds in some of these complexes are predominantly ionic, and measurements of thermoelectric power indicate that the charge carriers are predominantly negative.

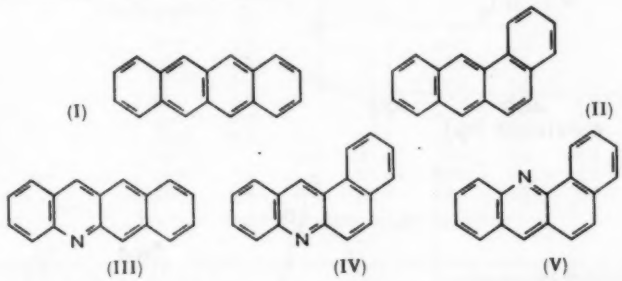
Implications of these results are discussed for models of polarisation bonding and of electrical conductance in solid aromatic complexes.

ELECTRONIC properties of aromatic compounds, particularly in the solid state, are attracting increasing attention (cf. review by Garrett [2]). In the present series of researches [1,3]

[1] Part VI, Parkyns and Ubbelohde, *J.*, 1961, 2110; cf. *J.*, 1960, 4188.
[2] Garrett in "Semiconductors," ed. N. B. Hannay, Reinhold Publ. Co., New York, 1959.
[3] Holmes-Walker and Ubbelohde, *J.*, 1954, 720; Gracey and Ubbelohde, *J.*, 1955, 4089; Slough and Ubbelohde, *J.*, 1957, 911, 918, 982.

special attention has been directed towards the effects of forming polarisation bonds * on the electronic properties.

Because of the nature of π-electron systems, most aromatic molecules show some amphoteric character. They can act as electron donors in complexes with acceptor groups such as bromine or iodine, and as electron acceptors with the alkali metals. Striking increases of electrical conductivity [1,3,6] have been found when polarisation-bond complexes are formed, and it is important to relate these in a systematic way with the structures of the parent aromatic molecules. Such investigations promise to throw light on polarisation bonding generally; they also give access to a group of semi-conductors and conductors with interesting properties. The researches recorded below refer to tetracyclic aromatic molecules. In order to study effects of molecular shape, naphthacene (I) and 1,2-benzanthracene (II) were selected as parent molecules which are fairly readily available. In order to study effects of electronic perturbations on these molecules, the aromatic aza-analogues 2,3- (III), 1,2- (IV), and 3,4-benzacridine (V) have been prepared in the pure state. Properties were also studied of preparative intermediates of benzacridine, namely, the chlorobenzacridines and benzacridones.



Polarisation-bond complexes have been prepared with iodine and with sodium. For comparisons between the various solids studied, polycrystalline materials have been used under compression. Their dark-current conductivities have been determined at various temperatures, for carefully purified solids. Preliminary measurements of thermoelectric power have been made in some cases to determine the sign of the predominant charge carriers. Mechanisms suggested for conductance processes in these solids are discussed below.

Because of the chemical interrelation between these aromatic systems, changes observed in the conductance parameters can to a considerable extent be correlated with structure. Further information about these correlations has been obtained from studies of the ultra-violet absorption spectra in solution, and from studies of the molecular volumes of the solid complexes.

Experimental

Source of Materials.—Naphthacene (I) (L. Light & Co.) and 1,2-benzanthracene (II) (Rutgerswerke A.G.) were purified as described below. 2,3-Benzacridine (III) was synthesised as described by Albert, Brown, and Duewell.[7] 9-Chloro-2,3-benzacridine and 2,3-benzacridone

* The general term " polarisation bond " (cf. McKeown, Ubbelohde, and Woodward [4]) may conveniently be used to describe a specific interaction between molecules forming this bond, in cases when this can be distinguished from the non-specific van der Waals attraction between molecules, and from primary covalent or ionic bonding. The term " charge transfer " bond refers to a particular theoretical interpretation of certain polarisation bonds, due to Mulliken.[5]

[4] McKeown, Ubbelohde, and Woodward, *Acta Cryst.*, 1951, **4**, 391.
[5] Mulliken, *J. Amer. Chem. Soc.*, 1950, **72**, 600.
[6] Akamatu, Inokuchi, and Matsunaga, *Bull. Chem. Soc. Japan*, 1956, **29**, 213; Kommandeur and Hall, *J. Chem. Phys.*, 1961, **34**, 129; Singer and Kommandeur, *ibid.*, p. 133.
[7] Albert, Brown, and Duewell, *J.*, 1948, 1284.

which occur as intermediates in this synthesis were also isolated and purified for physical measurements.

1,2-Benzacridine (IV) was synthesised from 9-chloro-1,2-benzacridine (cf. Bryant, Bachman, and Picha [8]) by reduction with lithium aluminium hydride.[9] 1,2-Benzacridone was also isolated and purified for physical measurements.

3,4-Benzacridine (V), 9-chloro-3,4-benzacridine, and 3,4-benzacridone were prepared by methods analogous to those used for the 1,2-isomer.

Purification of Materials.—Because of the small concentration of charge carriers present in many organic solids, their electrical properties can be particularly sensitive to the presence of comparatively minute concentrations of inorganic or organic impurities (cf. Parkyns and

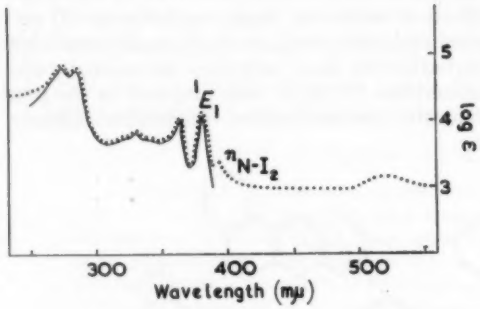


FIG. 1A: ——— 10^{-5}M-1,2-Benzacridine. ····· 10^{-5}M-1,2-Benzacridine plus 2 × 10^{-5}M-iodine.

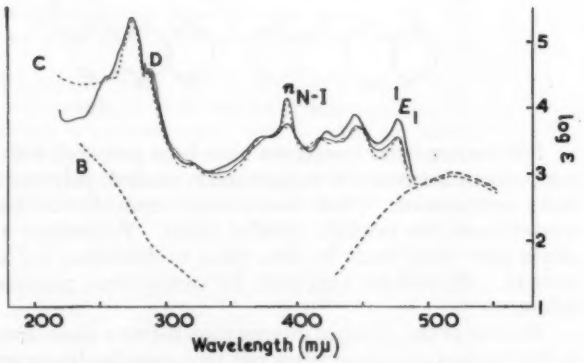


Fig. 1B: A, 10^{-5}M-2,3-Benzacridine. B, 10^{-3}M-Iodine. C, Complex from 10^{-5}M-2,3-benzacridine plus 10^{-3}M-iodine. D, Complex from 10^{-4}M-2,3-benzacridine and 10^{-4}M-iodine.

FIG. 1. Ultraviolet absorption spectra of carbon tetrachloride solutions.

Ubbelohde [1]). Suitable methods of purification of these comparatively large molecules depend on their physicochemical properties. The procedure adopted for all the present compounds except the benzacridones was as follows:

The substance was first recrystallised from ethanol or benzene until its m. p. was unchanged (within ±0·5°) by further crystallisation. The récrystallised material was passed in " AnalaR " benzene (dried over sodium) through a column (1¼" × 18") of alumina (Peter Spence Type H). The solid was separated from the solvent by vacuum-distillation and to ensure that limiting purification had been attained the chromatography was repeated with fresh benzene. Finally, vacuum-sublimation was used to remove the last trace of solvent. Owing to the low solubility of the benzacridones in convenient solvents, purification by chromatography was omitted for these substances. Vacuum-sublimation of the recrystallised material was repeated until the sublimate had the same m. p. within 0·5° as the material being sublimed.

Ultraviolet Absorption Spectra.—These were determined by means of a Hilger Uvispek model

[8] Bryant, Bachman, and Picha, *J. Amer. Chem. Soc.*, 1946, **68**, 1599.
[9] Cf. Badger, Pearce, and Pettit, *J.*, 1951, 3199, 3204.

H 700/302 with stoppered quartz cells, previously calibrated. For the parent molecules, these spectra provided a check on the purity and indicated the wavelength of the peak absorption for the transition of lowest energy. Absorption spectra were also investigated for solutions of the aromatic hydrocarbons and bases in carbon tetrachloride (B.D.H. " special for spectroscopy "), to which iodine had been added in 1 : 1 molar ratio. These solutions were prepared by dissolving weighed amounts of the organic material and of resublimed iodine, whilst oxygen was excluded by bubbling dry nitrogen through the solvent. The vessel was shielded from direct light. The solutions were diluted to 10^{-5}M and matched against three check cells containing, respectively, the pure solvent, an equimolar solution of the aromatic substance, and an equimolar solution of iodine. Some characteristic absorption spectra are plotted in Figs. 1A and B.

Preparation of Solid Complexes with Iodine.—An equimolar solution of the hydrocarbon (0·228 g.) and of iodine (0·257 g.) in carbon tetrachloride (100—150 ml.) was prepared by bubbling dry oxygen-free nitrogen (cf. Part VIII) through the mixture. The solvent was then

TABLE 1.

Analyses of complexes with iodine, ArI_m.

	Found (%)				1 : 1 Molecular complex requires for Calc. (%) for $m = 1$				
Ar	C	H	N	I	C	H	N	I	*m*
Naphthacene *	47·3	2·6		51·4	44·0	2·5		52·6	1·78
3,4-Benzanthracene *	47·7	2·7		49·8	44·0	2·5		52·6	1·74
2,3-Benzacridine	42·35	2·4	2·95	52·4	42·3	2·3	2·9	52·5	2·0
2,3-Benzacridone	55·0	2·9		33·3	40·8	2·2	2·8	51·0	1·30
9-Cl-2,3-Benzacridine	45·3	2·2		42·3	39·4	1·9	2·7	49·1	1·74
1,2-Benzacridine	42·45	2·6	3·0	52·4	42·3	2·3	2·9	52·5	2·0
1,2-Benzacridone	56·75		3·4	31·6	40·8	2·2	2·8	51·0	1·26
9-Cl-1,2-Benzacridine	44·9	2·2		42·05	39·4	1·9	2·7	49·1	1·72
3,4-Benzacridine	43·3	2·6	2·7	51·3	42·3	2·3	2·9	52·5	1·76

* Direct addition of iodine and weighing.

evaporated completely at room temperature under a moderate vacuum in a slow stream of nitrogen. Analytical checks of the compositions of the resulting solids (Table 1) point to some loss of iodine from those complexes in which it is only weakly held. This probably occurred during evaporation or during handling. Complexes with 2,3- and 1,2-benzacridine and with their chloro-derivatives retained iodine more strongly and gave analyses close to the theoretical 1 : 1 formula.

Preparation of Solid Complexes with Sodium.—This was carried out as described in the following paper, which also gives details for handling of these reactive materials.

Compositions of the alkali-metal complexes (Table 2) were determined by weighing, decom-

TABLE 2.

Analyses of sodium adducts, $ArNa_m$.

	Found (%)			Calc. (%) for $m = 1$ or 2			
Ar	C + H	N	Na	C + H	N	Na	*m*
Naphthacene	84·8		15·2	83·2		16·8	1·80
3,4-Benzanthracene	91·55		8·45	91·6		8·4	1·02
2,3-Benzacridine		91	9·0		91·6	8·4	0·93
1,2-Benzacridine		83·3	16·7		83·2	16·8	1·99
3,4-Benzacridine		83·5	16·5		83·2	16·8	1·97

position in aqueous ethanol, and titration against hydrochloric acid.

Conductivity.—This was measured for compressed polycrystalline material. The parent substance or a complex freshly prepared and stored under nitrogen was made into a pellet at room temperature in a screw press exerting about 200 kg./cm.^{2}. The pellet was transferred by extrusion to a conductivity cell either in a protective nitrogen box (cf. following paper) or under protection of a flow of nitrogen. With the parent substance and its complexes with iodine, a number of measurements were made by carrying out all these operations in air instead of under nitrogen: no significant change was observed in the conductance parameters, indicating that oxygen had a negligible effect. With sodium complexes, access of air led to rapid and sometimes violent reaction and all operations were fully protected by nitrogen.

Values of the specific conductivity σ are given in Tables 3 and 4 which record the parameters defining straight-line logarithmic plots of the results, according to the equation $\sigma = \sigma_0 \exp -\varepsilon/kT$. For intrinsic semiconductors the energy gap $\Delta\varepsilon = 2\varepsilon$. Illustrative logarithmic plots are shown in Figs. 2, 3, 4, and 5. Thermoelectric power (T.E.P.) was measured as described in the following paper.

Densities were measured by conventional pyknometry, with precautions against access of air or moisture (cf. following paper). Values are recorded in Tables 5a and b. These Tables

TABLE 3.

Conductance parameters of aromatic complexes with iodine (ArI_m) at 30°.

Ar	m	σ (10^{-12} ohm^{-1} cm.$^{-1}$)	log σ_0	ε (ev)	T.E.P. of complex (μv/°c)
Naphthacene	—	0·7	1·0	0·8	
,, + I_2 ...	1·76	100	−0·85	0·55	Small +ve
1,2-Benzanthracene ...	—	0·0001	1·3	1·04	
,, + I_2	1·74	1·0	2·98	0·90	Small +ve
2,3-Benzacridine	—	0·0008	−1·3	0·83	
,, + I_2	2·0	950·0	10·0	1·2	+350
2,3-Benzacridone	—	0·003	−6·2	0·5	
,, + I_2	1·3	790·0	7·5	1·0	+250
9-Cl-2,3-Benzacridine	—	0·002	−1·4	0·7	
,, + I_2	1·72	0·19	8·10	1·25	+330
1,2-Benzacridine	—	0·0007	2·3	1·05	
,, + I_2	2·0	0·018	9·65	1·4	+370
1,2-Benzacridone	—	0·0007	−6·4	0·53	
,, + I_2	1·26	200	1·9	0·70	+190
9-Cl-1,2-Benzacridine	—	0·003	−1·2	0·80	
,, + I_2	1·72	0·15	6·2	1·15	+300
3,4-Benzacridine	—	0·001	4·5	1·18	
,, + I_2	1·76	1·2	3·88	0·95	Small +ve

TABLE 4.

Conductance parameters of aromatic complexes with sodium, $ArNa_m$, at 30° (for the parent compounds see Table 3).

Ar	m	σ (10^{-12} ohm^{-1} cm.$^{-1}$)	log σ_0	ε (ev)	T.E.P. of complex (μv/°c)
Naphthacene	1·8	42,000	−2·06	0·32	Negative, ~10
1,2-Benzanthracene	1·02	110	1·03	0·66	Negative, small
2,3-Benzacridine	0·93	1900	5·76	0·87	Negative, small
1,2-Benzacridine	1·99	90	−1·73	0·50	Negative, small
3,4-Benzacridine	1·97	1800	−3·26	0·33	Negative, small

TABLE 5.

(a) Molar volumes (c.c) of iodine complexes ArI_m.

Ar	Parent Density (g./c.c.)	Parent M.V. (c.c.)	Complex Density (g./c.c.)	Complex M.V. (c.c.)	Δ (c.c.)	m
Naphthacene	1·40	163	2·21	204	5·0	1·78
1,2-Benzanthracene	1·28	178	2·08	216	7·0	1·74
2,3-Benzacridine	1·42	161	1·98	243	−31·0	2·0
2,3-Benzacridone	1·41	173	2·08	197	9·0	1·30
9-Cl-2,3-Benzacridine	1·30	202	1·85	260	−14	1·72
1,2-Benzacridine	1·29	177·5	2·38	202	27·0	2·0
1,2-Benzacridone	1·39	175	2·05	198	9·0	1·26
9-Cl-1,2-Benzacridine	1·34	196	2·27	212	29·0	1·74
3,4-Benzacridine	1·24	184	2·06	219	10·0	1·76
Iodine (per atom)	4·94	25·7	—	—		

Δ = Theor. molar volume (no interaction between donor and acceptor) − obs. molar volume. Δ is positive if a contraction has occurred.

(b) Molar volumes (c.c.) of sodium complexes $ArNa_m$.

Ar	Mol. vol. (c.c.)	Δ	m	Ar	Mol. vol. (c.c.)	Δ	m
Naphthacene	195	15·4	2	1,2-Benzacridine	201	24	2
1,2-Benzanthracene ...	203	−1	1	3,4-Benzacridine	211	20	2
2,3-Benzacridine	184	1	1	Sodium (metal)	23·7		

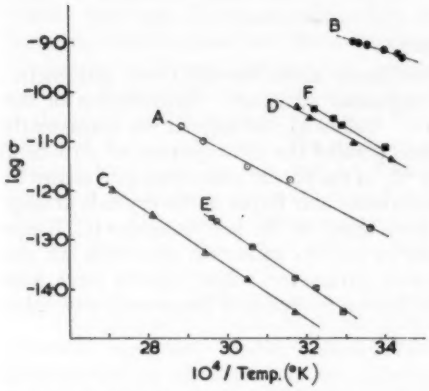


FIG. 2: A, Naphthacene. B, Naphthacene + I_2. C, 1,2-Benzanthracene. D, 1,2-Benzanthracene + I_2. E, 3,4-Benzacridine. F, 3,4-Benzacridine + I_2.

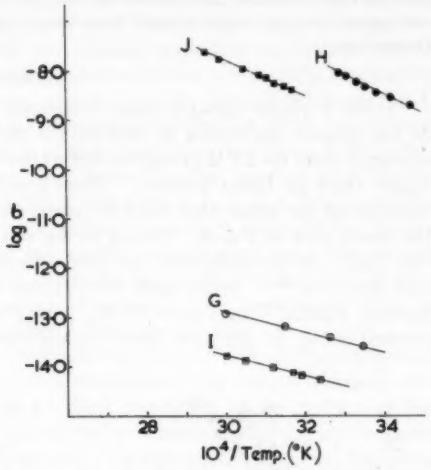


FIG. 3: G, 2,3-Benzacridone. H, 2,3-Benzacridone + I_2. I, 1,2-Benzacridone. J, 1,2-Benzacridone + I_2.

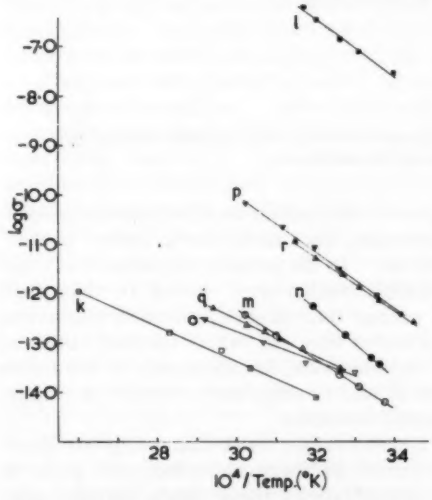


FIG. 4: K, 2,3-Benzacridine. L, 2,3-Benzacridine + I_2. M, 1,2-Benzacridine. N, 1,2-Benzacridine + I_2. O, 9-Chloro-2,3-benzacridine. P, 9-Cloro-2,3,-benzacridine + I_2. Q, 9-Chloro-1,2-benzacridine. R, 9-Chloro-1,2-benzacridine + I_2.

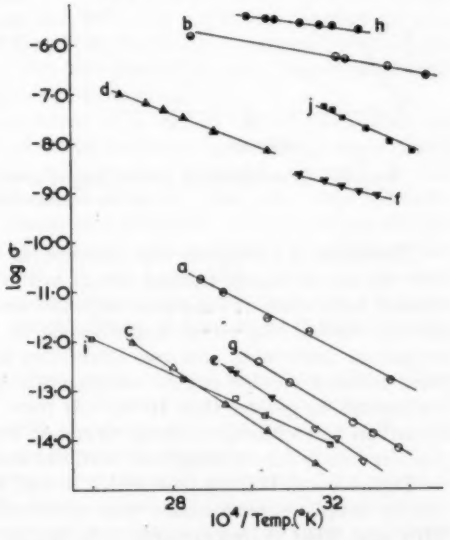


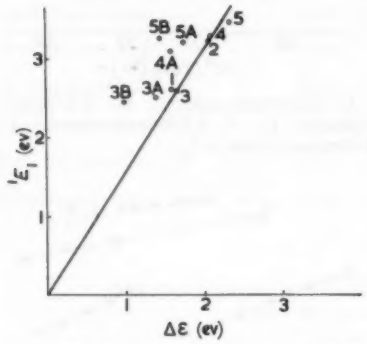
FIG. 5. Conductivities of sodium complexes and parent molecules. a, Naphthacenes b, Naphthacene + 2Na. c, 1,2-Benzanthracene. d, 1,2-Benzanthracene + Na. e, 3,4-Benzacridine. f, 3,4-Benzacridine + 2Na. g, 1,2-Benzacridine. h, 1,2-Benzacridine + 2Na. i, 2,3-Benzacridine. 2,3-Benzacridine + Na.

FIGS. 2—4. Conductivities of iodine complexes and parent molecules.

include the difference Δ between the sum of the molar volumes of the reactants, and the molar volume of the complexes formed from them; positive values of Δ imply a shrinkage on complex formation.

Discussion

Table 3 yields directly some systematic conclusions about the electronic parameters of the parent molecules in relation to their molecular structure. Substitution of one nitrogen atom for a CH group has little effect on ε. Values of ε for angular are consistently higher than for linear isomers. These conclusions parallel the consequences of structural changes on the absorption band of lowest energy $^1E_1$ of the parent molecules, as is shown by the linear plot in Fig. 6. Owing to the weak intermolecular forces in the crystals absorption bands for the solids are not very different from those for the free molecules (cf. Kasha and McGlynn [10]). Since both the electron affinities and the ionisation potentials are also linearly related [11] to values of $^1E_1$, either of these parameters might equally have been plotted in Fig, 6; they are, however, not directly known for many of the present molecules.



1, Naphthacene. 2, 1,2-Benzanthracene. 3, 2,3-Benzacridine. 3A, 9-Chloro-2,3-benzacridine. 3B, 2,3-Benzacridine. 4, 1,2-Benzacridine. 4A, 9-Chloro-1,2-benzacridine. 5, 3,4-Benzacridine. 5A, 9-Chloro-3,4-benzacridine. 5B, 3,4-Benzacridone.

Fig. 6. Correlation of lowest singlet absorption level $^1E_1$ with intrinsic energy gap Δε for conduction of the solids.

Formation of Complexes with Electron Acceptors.—Measurements of ultraviolet absorption can reveal charge-transfer complexes in solution, since these should have "peaks" distinct from those of the parent aromatic molecule. In the present researches this could not be verified for either naphthacene or 1,2-benzanthracene. Owing to their high extinction coefficients and low solubilities in carbon tetrachloride, solutions containing these molecules could not be conveniently measured over the whole spectral range, at concentrations greater than 10^{-5}M. At these concentrations, the absorption of free iodine in carbon tetrachloride extends to about 2600 Å and swamps any evidence of charge-transfer bands due to complexes with the aromatic molecules.

Figs. 1A and B show that with 2,3- and 1,2-benzacridine, weak charge-transfer bands due to complexes with iodine were observed even at 10^{-5}M-concentration, with peaks at 3970 and 3940 Å respectively. At higher concentrations these bands become more prominent. They may be attributed to ^nN–I_2 interaction between the iodine molecule and the aromatic base, since they occur in the spectral region expected for this. The absorption spectrum of acridine hydrochloride is analogous with that of the complex between acridine and bromine.[12] Charge-transfer absorption peaks for complexes between halogens and other monoaza-aromatic molecules also lie in this region of wavelengths.[12,13]

[10] Kasha and McGlynn, *Amer. Rev. Phys. Chem.*, 1956, **17**, 407.
[11] Matsen, *J. Chem. Phys.*, 1956, **24**, 602.
[12] Acheson, Hoult, and Barnard, *J.*, 1954, 4142.
[13] Chaundhuri and Basu, *Trans. Faraday Soc.*, 1959, **55**, 898.

Further support for the $^{n}N–I_2$ attribution is provided by the present finding that whereas both 2,3- and 1,2-benzacridine complexes with iodine give these absorption peaks, that with 3,4-benzacridine fails to do so. Scaled repulsion envelopes around molecular models show that the nitrogen atom in 3,4-benzacridine is sterically blocked by the hydrogen atom of the angular benzene ring adjacent to it. In this instance the I_2 molecule cannot approach sufficiently close to nitrogen to give effective $^{n}N–I_2$ interaction in the plane of the aromatic system. Properties of the crystalline complexes with iodine bear out this conclusion. The analyses show that iodine is only weakly held by the homonuclear hydrocarbons and by 3,4-benzacridine, whereas 2,3- and 1,2-benzacridine and their chloro-derivatives retain iodine strongly, giving complexes with definite m. p.s (2,3- 158°; 3,4- 165°). Molar volumes (Table 5a) again indicate very weak interaction for complexes between iodine and the first three aromatic molecules, but marked electrostriction for 1,2-benzacridine. For the 2,3-benzo-compounds the expansion may be attributed to salt formation giving 2,3-benzacridine N-iodonium iodide.

Differences in the conductance parameters run parallel with these differences in physicochemical properties. Table 3 shows that complex-formation with iodine increases the conductivity in all cases, but the influence on ε differs according to the nature of the bonding. Where the (weak) interaction may probably be described as $\pi–I_2$, ε is lowered on passing from the parent molecule (naphthacene, 1,2-benzanthracene, or 3,4-benzacridine) to the complex with iodine. On the other hand, for strong interactions (2,3- and 1,2-benzacridine, etc.) ε is increased on passing to the complex.

Values of thermoelectric power (T.E.P.) were readily measurable in many cases; they were positive with respect to the cold junction, indicating that the majority of carriers of electricity are positive. Observed values around 300—400 μV/°C are comparable with those of inorganic semiconductors. For $\pi–I_2$ complexes, T.E.P.'s are much smaller but also positive. Accurate values could not be obtained except by using large temperature differences, at which decomposition of the complex took place.

Complexes with Electron Donors.—Results listed in Tables 4 and 5b show that the behaviour of complexes between tetracyclic aromatic molecules and alkali metals closely resembles that reported for similar complexes with smaller aromatic systems.[3] It was interesting that only monosodium derivatives of 1,2-benzanthracene and 2,3-benzacridine were formed even after prolonged ultrasonic activation. For these, the electrostriction is also much smaller (Table 5b). Naphthacene, 1,2- and 3,4-benzacridine readily gave disodium derivatives. Although present lack of knowledge about the electron affinity of aromatic mononegative ions obstructs definitive interpretation of this difference, it is interesting that the lower homologues acridine [3] and phenanthrene [14] likewise form only monosodium derivatives in solution.

Conductance parameters (Tables 3 and 4) show that complex formation with sodium lowers the specific resistance by a factor of 10^6—10^8 in all cases. In all instances the thermoelectric power was small and was negative with respect to the cold junction, indicating that most of the carriers in these complexes are negatively charged.

In solution, ultraviolet-absorption spectra and reduction potentials, as measured, point to the presence of negative ions of the hydrocarbons (cf. Hoijtink [14,15]) which are also indicated from measurements on electron-spin resonance of monosodium complexes in ethereal solvents.[16] Molar volumes (cf. Table 5b) indicate a predominantly ionic character of the solids. Conductance parameters of these complexes appear to be less sensitive to individual molecular structure in this group of aromatic molecules than for corresponding complexes with electron acceptors.

Conduction Mechanisms in the Parent Aromatic Hydrocarbons.—On the basis of LCAO MO calculations for fused aromatic hydrocarbons the ultraviolet absorption band $^1E_1$ of

[14] Hoijtink, *Rec. Trav. chim.*, 1957, **76**, 813.
[15] Hoijtink, *Rec. Trav. chim.*, 1954, **73**, 355; 1955, **74**, 277; 1956, **75**, 487.
[16] Lipkin, Paul, Townsend, and Weissman, *Science*, 1953, 117, 534.

longest wavelength is attributed to excitation of an electron from the highest filled π-bonding orbital to the lowest empty π^*-antibonding orbital within the same molecule (cf. Coulson [17]). For the heterocyclic molecules, the absorption band of longest wavelength is attributed to a $^nN \longrightarrow \pi$ transition, in which the ground state is associated with a nitrogen atom. Normally, substitution of nitrogen for CH in the ring shifts the absorption edge to longer wavelengths, by about 15 mμ. If the correlation between $\Delta\epsilon$ and $^1E_1$ indicated by the linear plot of Fig. 6 for the parent molecules is significant, this mode of excitation could provide a clue to the mechanism controlling conduction. Alternatively, a correlation has also been proposed [18] between $\Delta\epsilon$ and the excitation energy to the first triplet level $^3E_1$. This transition is, however, strongly forbidden in the free molecule, and in the absence of strong perturbations in the crystal its contribution to the conduction mechanism seems rather less likely.

Primary thermal excitation of the pure hydrocarbon either to the $^1E_1$ or to the $^3E_1$ state in the crystal could not produce charge carriers directly. Such excitation could become the controlling mechanism, if there were a directly linked consecutive process in the solids leading to conduction. Since the centres of the molecules are fixed in the crystals one possibility is that " tunnelling " of electrons occurs much more readily between neighbouring molecules in the excited and the ground state than between two molecules in the ground state because of the increase in effective molecular size on excitation. Another possibility is that the excited states wander through the crystal as " excitons " with little or no thermal degradation, until they encounter special defect sites in the crystal where an electron can be trapped, leaving a positive charge carrier which migrates when a field is applied. The positive sign of the charge carriers for both dark-current and photocurrent measurements (Chynoweth and Schneider [19]) lends some support to the second possibility, which may also help to explain the behaviour of charge-transfer complexes discussed below.

A third possibility is that direct thermal excitation to ionised states of the aromatic molecule in the crystal provides the mechanism controlling conduction. Thus in anthracene [20] the energy required to transfer an electron from any molecule to a region remote from it in the crystal is about 3·0 ev, compared with the ionisation energy of the free molecule [11] of about 7·23 ev. But if the electron is merely transferred to a neighbouring molecule, creating an ion pair, $(Ar^-)(Ar^+)$, this requires only about 2·2 ev (ref. 9) which is close to observed values for $\Delta\epsilon$ of 1·97 ev. Even ion pairs would not provide charge carriers directly, but their interaction with neighbouring aromatic molecules in the crystal could lead to a narrow conduction band (cf. Fox [21]). If an electric field is applied to crystals containing ion pairs, then, when the strain becomes sufficiently large, additional charge carriers could result by disruption and could lead to non-ohmic conductance. However, a lower limit to the field strength required appears to lie around 10^3 v/cm. In the present experiments we used fields not exceeding 200 v/cm., and conductance was ohmic throughout (cf. following paper).

The Effect of Substitution on the Conductance Parameters.—As seen from Fig. 6, chlorobenzacridines have a markedly lower thermal-energy gap than their parents. By analogy with the ultraviolet spectra of the molecule in solution, a small lowering in $\Delta\epsilon$ might be expected, owing to the bathochromic effect of chloro-substitution, but in the solid state the effect on the energy gap is much more striking.

Craig and Hobbins [22] showed that the electronic transitions in the solid state depend largely on intermolecular vibrational interactions and multipole electrostatic interactions.

[17] Coulson, " Valence," Clarendon Press, Oxford, 1952.
[18] Northrop and Simpson, *Proc. Roy. Soc.*, 1956, *A*, **234**, 124.
[19] Chynoweth and Schneider, *J. Chem. Phys.*, 1954, **22**, 1021.
[20] Lyons, *J.*, 1957, 5001.
[21] Fox, *J. Phys. Chem. Solids*, 1959, **8**, 439.
[22] Craig and Hobbins, *J.*, 1955, 539, 2309.

Many strong transitions in the free molecule are weakened in the solid in favour of the low-probability transitions; there are other changes of low-energy transitions in the solid state even at liquid-helium temperatures. Since the vibrational characteristics of the chloro-substituent are markedly different from those of the hydrogen it replaces, and since larger dipole and multipole moments probably occur for a chloro-substituent, it is to be expected that chloro-substitution affects electronic transitions in the solid much more markedly than in the free molecule. Formation of ion-pair crystal states is likely to depend on near-neighbour molecular interactions similar to those of the parent molecules, so that chloro-substitution can produce marked lowering in the thermal excitation required for conduction. This probably also explains why the bulk photocurrent for chloro-anthracene is larger than for anthracene.[23]

For the benzacridones, where the lowering of thermal excitation energy (Fig. 6) is even greater than for the the chloro-isomers, similar considerations may apply. There is also the possibility of proton migration in the crystals by way of nitrogen, hydrogen, and oxygen bridges, but no other evidence has yet been obtained to suggest that at low field strengths (~200 v/cm.) the currect might in part be carried by such means.

Conduction Mechanisms in Solid Polarisation-bond Complexes.—The ion-pair model of thermal activation for conduction in pure hydrocarbons described above is supported by the consideration that addition complexes between aromatic molecules and either electron acceptors or electron donors are likely to yield ion pairs in much greater concentration than could be produced by mere thermal excitation of the parent molecules.

For complexes with electron acceptors, the electrostriction of molar volumes is generally small (Table 5a), and a similar description of conductance starting from ion pairs is probably still useful. With electron donors such as sodium, the strong co-operative interaction in the crystals indicated by the electrostriction (Table 5b) suggests that electron levels of the aromatic molecules must be profoundly perturbed; probably they are broadened and fused, to give new energy bands for the crystals, resembling those for metals or intermetallic semi-conductors.

One of us (G. C. M.) thanks the Institute of Petroleum (Hydrocarbon Panel) for a research bursary.

Department of Chemical Engineering and Chemical Technology,
Imperial College of Science and Technology,
London, S.W.7. [*Received, April 24th*, 1961.]

[23] Lyons, Bree, and Morris, Proc. 3rd Carbon Conf., Pergamon Press, London, 1959, 87.

976. *Electron-donor and -acceptor Complexes with Aromatic Systems. Part VIII.*[1] *Preparations and Physical Measurements of New Metal Addition Complexes with Aromatic Systems in the Solid State.*

By G. C. Martin, N. D. Parkyns, and A. R. Ubbelohde.

The electrical properties of metal–aromatic complexes ArM_m in the solid state can be extremely sensitive to contamination by oxygen, moisture, or carbon dioxide. Methods of preparation of such complexes are detailed which ensure their complete protection from the atmosphere.

As one example, tetracyclic aromatic molecules are described which are sufficiently soluble in low-boiling ether solvents to allow preparation of complexes by ultrasonic activation of their solutions in contact with the free metal. Larger aromatic systems, for example, those with 9 fused rings, are not sufficiently soluble to permit this. Since the vapour pressure of the latter at ~400° is low, the complexes can be formed by diffusion of the metal vapour into the polycrystalline aromatic solid. This procedure is described for preparations of sodium and potassium complexes with isoviolanthrene.

Operations involving transfer into measurement cells or into weighing bottles have to be carried out in an inert atmosphere. A glove box for this purpose is described which incorporates a sodium-arc purifier to scavenge any atmospheric gases diffusing through the gloves.

Cells for measuring conductivity and thermoelectric power suitable for use in such a box are also illustrated.

Previous methods[2,3] of preparation of addition complexes of aromatic hydrocarbons with alkali metals have often relied on refluxing or stirring a solution of the organic compound in dry ether or another solvent, in contact with the free metal. This operation can require several days to afford complexes with a high content of metal atoms. During this time traces of oxygen or moisture can diffuse into the reaction solution to an appreciable extent, even when the solution is protected by nitrogen. Resulting products of oxidation may be sufficient to modify the electrical properties of the solid complex. Slough and Ubbelohde[4] gave a preliminary description of a method using ultrasonic activation of the solution to accelerate complex formation by the benzoquinolines in ethereal solvents. This method has now been extended, with a number of improvements, to the preparation of sodium complexes of the tetracyclic molecules, naphthacene, 1,2-benzanthracene, and 2,3-, 3,4-, and 1,2-benzacridine.

Molecules with more fused rings are, however, only slightly soluble in ethers with a low C : O ratio,[3] and this limits the usefulness of ultrasonic methods of preparation. Such molecules have high melting points and high sublimation temperatures, which facilitates the formation of their alkali-metal addition complexes by diffusion of the metal vapour into the solid at 400—450° in a high-vacuum system. Sodium and potassium complexes of isoviolanthrene have been prepared by this means.[5]

Experimental

Nitrogen (B.O.C. "White Spot"; $O_2 < 10$ p.p.m.) was purified from oxygen by passage (about 100 c.c./min.) through a column, 3 cm. in diameter and 200 cm. in length, containing copper turnings freshly reduced in hydrogen at 500°. The column was maintained at 490—510° along its length. The issuing gas was then freed from water vapour by passage through

[1] Part VII, Martin and Ubbelohde, preceding paper.
[2] Holmes-Walker and Ubbelohde, *J.*, 1954, 720.
[3] Scott, Walker, and Hansley, *J. Amer. Chem. Soc.*, 1936, **58**, 2442.
[4] Slough and Ubbelohde, *J.*, 1957, 918.
[5] Parkyns and Ubbelohde, *J.*, 1961, 2110.

100% sulphuric acid, baked-out soda lime, and two traps packed with glass wool and cooled in liquid air.

Subsequent references to " nitrogen " refer to gas treated in this way.

Purification of Materials.—The aromatic tetracyclic hydrocarbons or bases were purified by the procedure as described in the previous paper. Isoviolanthrene is chemically less stable and was purified by the procedure adopted by Parkyns and Ubbelohde.[6] Dioxan, used in the preparation of the alkali-metal complexes of the tetracyclic aromatic systems, was refluxed with sodium until the metal remained bright, and twice distilled from bright sodium against a counter-current of nitrogen; the distillate was kept under nitrogen; it was pale blue, probably owing to dissolved sodium.[7]

Preparation in Ether-type Solutions.—Solutions of the tetracyclic aromatic hydrocarbons and bases reacted with sodium on ultrasonic activation. The ultrasonic probe and reaction cell are shown in Fig. 1. The purified hydrocarbon (0·5 g.) was added to the cell which was kept protected by a stream of nitrogen; purging with nitrogen was continued for a further

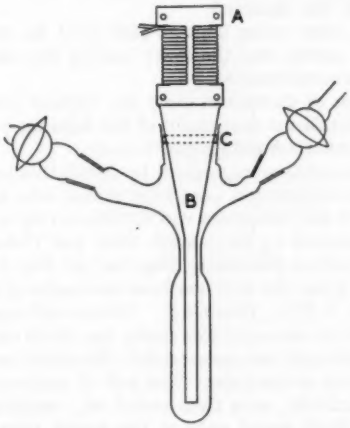


FIG. 1. Ultrasonic activator and reaction cell.

half-hour. Dioxan (15 ml.) was distilled into the vessel against the flow of nitrogen and a " pea " of bright sodium (kept in purified dioxan under nitrogen) was then added to the vessel. The colour of the aromatic mononegative ion appeared immediately on the surface of the sodium. The ultrasonic probe was then inserted slowly against the counter-flow of nitrogen and was fixed at the nodal position by a Neoprene gasket (C) which provided a gas-tight seal to the Pyrex-glass reaction vessel. The probe was vibrated by means of a transducer head (A) brazed to the stainless-steel tapered shaft (B) which was $8\frac{1}{2}''$ long and $1\frac{1}{4}''$ in diameter at the head going to $\frac{1}{4}''$ diameter at the lower end. The transducer was a Mullard $1'' \times 1\frac{1}{4}''$ laminated " Permandur " magnetostrictor with a maximum power output of 2 kw. Although the mica interleaving reduces power losses due to eddy-current effects, it was necessary during operation to cool the head by forced convection with an air-blower. The energy to drive the magnetostrictor was obtained from an oscillator and a power amplifier to give 100 v output at a frequency of 20—30 kc./sec.; coupled to this was a D.C. polarizing current of 6 A at 10—25 v.

The alternating-current output was tuned to give maximum resonance with the magnetostrictor at 25 kc./sec. Although 1000 w could be supplied to the transducer, under normal operation only 400—600 w were necessary to bring about complete reaction. This high efficiency was helped by the tapered design of the probe and the narrow reaction cell. After 5—10 minutes' activation the whole solution attained the colour of the complex. During further activation of the benzacridines a number of different colour changes were observed which bore no obvious relation to the ultimate composition attained (as found by analysis).

[6] Parkyns and Ubbelohde, *J.*, 1960, 4188.
[7] Down, Lewis, Moore, and Wilkinson, *Proc. Chem. Soc.*, 1959, 209.

It seems likely that these colour changes were due to self-complex-formation, between benzacridine which had not yet reacted and its mono- or di-negative ion. Prolonged ultrasonic activation (2 hr.) was necessary in order to afford the disodium derivatives of naphthacene and 1,2- and 3,4-benzacridine. However long the reaction, at the concentrations used only the monosodium derivative of 2,3-benzacridine and 1,2-benzanthracene could be prepared.

Solid complexes were obtained solvent-free by transferring the reaction vessel, after removal of the probe, to a high-vacuum line flushed with nitrogen. The whole was cooled in liquid nitrogen and the system evacuated to 10^{-4} mm. of mercury. The vacuum system contained two traps cooled by liquid nitrogen to collect the dioxan which evaporated from the complex as the temperature was slowly raised. When the powder was dry the temperature was raised to 180° to remove any strongly held dioxan. In preliminary experiments, where complex formation had not been taken to completion, some hydrocarbon sublimed from the powder at this temperature, but when formation of either the mono- or the di-sodium complex had been completed no sublimation could be observed. In a number of cases the temperature was raised to 500°; except for some darkening or charring near the limiting temperature no decomposition was observed.

Normally, after being kept at 180° for 1 hr. for removal of the last traces of dioxan, the complex was sealed into the lower half of the reaction cell at the constriction, until it was required for measurements.

Preparation of Complexes from the Vapour Phase.—To afford isoviolanthrene complexes with alkali metals use was made of the high m. p. and sublimation temperature, by treating the solid hydrocarbon with metal vapour.

The alkali metals were purified by distillation under a high vacuum, to remove hydrocarbon oils and gross impurities, and were sealed into ampoules containing about 0·5 g. of metal. Preparation of the complexes was carried out by a modification of the method of Fredenhagen and Suck,[8] adapted by McDonnell, Pink, and Ubbelohde.[9] The materials were contained in a tube similar to that previously described (cf. Fig. 2 of Part VI). Because alkali-metal vapours attack Pyrex glass, the reaction tube was made of soda glass with a protective layer flashed-on (NA 10 glass, G.E.C., Wembley). Whilst still open, the reaction tube was flushed with dry nitrogen, and the ampoule containing the alkali metal was cracked and placed in its open end. After this open end had been sealed, the alkali metal was distilled under a vacuum into the adjacent section of the tube. The pair of sections containing the alkali metal and the hydrocarbon, respectively, were then sealed off; reaction was brought about by placing the hydrocarbon and alkali metal ends of the sealed tube in two different furnaces. Different temperatures and reaction times were used for different preparations; in a typical preparation the hydrocarbon was heated at 450° and the potassium at 430° for 30 hr. Both ends of the tube were then allowed to remain at 400° for a further 12 hr. and the potassium tube was then sealed off. The distribution of alkali metal in the powder was allowed to reach uniformity during a further 24 hours' heating at 400°.

Unless otherwise stated, all operations involving transfer of the solid complexes were carried out in a nitrogen-filled dry box.

Construction of Dry Box.—This box was modified from a commercially available glove box (John Bass & Co.) of about 8 cubic ft. capacity. The principal change was to introduce a scavenging device, based on the ideas of Gibb,[10] for removing traces of oxygen or water that may enter during the operations at leaks or by diffusion through the rubber gloves. A continuous circuit of brass pipe, 2″ in diameter, was constructed underneath the box with its inlet and outlet at opposite sides. Nitrogen was forced round this circuit and through the box by a concentric centrifugal fan (Airmax Ltd.). A gas-tight brass pot, about 8″ in diameter, was inserted in the middle of the circuit beneath the box. One electrode, whose height could be adjusted, protruded through the detachable lid of the pot and another through its side. The side electrode was connected by a piece of copper wire to a porcelain dish containing solid sodium and placed inside the pot. An arc was struck by applying about 1000 v A.C. between the sodium in this dish and the top electrode; the current (about 1 A) was controlled by a choke of nominal 5 H inductance. By running this sodium arc continuously any access of oxygen or moisture to the box could be rapidly scavenged. At the beginning of an experiment, the dry

[8] Fredenhagen and Suck, *Z. anorg. Chem.*, 1929, **178**, 353.
[9] McDonnell, Pink, and Ubbelohde, *J.*, 1951, 191.
[10] Gibb, *Analyt. Chem.*, 1957, **29**, 584.

box was filled with nitrogen by inflating a large metereological balloon (500 g. size) inside the box and then deflating it by admitting nitrogen to the box itself. The mouth of this balloon was accessible from the outside. This operation was repeated, after which the sodium arc was operated continuously to remove remaining traces of air or water. Initial conditioning of the box required 7—14 days. To minimise diffusion of oxygen from the outside, the inside of the box was kept at a positive pressure of pure nitrogen (30—40 mm.). When they were not in use, the glove holes were sealed by metal discs over rubber gaskets. The purity of the internal atmosphere was indicated by the length of time a freshly exposed piece of sodium remained bright. Under favourable conditions, manipulations could be completed in about 10 min.; perceptible tarnishing of freshly cut bright sodium might occur in about 1 hr.

Measurements of Density of Complexes.—These were made by means of a 10 ml. density bottle with liquid paraffin as densometric liquid. This paraffin was purified by bubbling pure nitrogen for a few hours through it at 120°. The complex (0·1—0·2 g.) was added to the density bottle, the stopper replaced, and the whole weighed. The complex was then quickly covered with paraffin and the bottle warmed to about 50° to remove entrapped nitrogen, then cooled

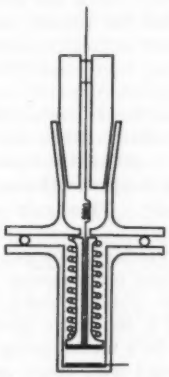


FIG. 2. Conductivity cell.

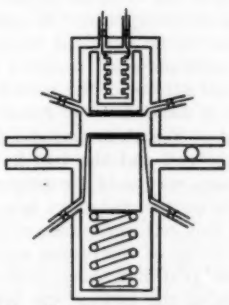


FIG. 3. Cell for measurement of thermoelectric power.

to 20°, filled completely with paraffin, and reweighed. The density of the complex was calculated in the usual way.

Measurement of Dark Resistance of Complexes.—A press was used for preparing pellets, 1—2 mm. thick, of the sample (cf. Parkyns and Ubbelohde [6]).

The special cell (Fig. 2) permitted subsequent measurements of resistance to be made outside the dry box. The central platinum lead was sealed with " Araldite " to prevent ingress of air, and was insulated by a hollow silica rod and silica stopper from the outside walls of the cell which were made of Pyrex glass. The use of silica enabled the resistance of compounds of the order of 10^{16} ohm cm. to be made if necessary (see preceding paper). The internal spring kept sufficient pressure (about 2 kg./cm.^{2}) on the platinum electrode to obviate surface contact effects arising from insufficient applied pressure on the pellet.

Most complexes gave satisfactory and cohesive pellets when a screw press was used.[6] It was impracticable to give them the annealing treatment described for isoviolanthrone and isoviolanthrene, but this was unnecessary largely because of the very much lower resistance of the complexes. Particularly with isoviolanthrene a few of the complexes rich in alkali metal never gave cohesive pellets. Possibly, like some metal powders, they require higher pressures than can be obtained from a hand press. Fortunately such complexes all gave pellets with very low electrical resistances ($\leqslant$100 ohms); any dependence of activation energy on pressure appears to be within the experimental error of the present experiments.

After making and insertion of the pellet, the cell was assembled in the dry box and was tightened by means of circular clamps over a rubber O-ring. In this cell the pellets gave reproducible values of electrical resistance outside the dry box for at least 2 days.

Resistances were measured in the temperature range 30—100° in a copper air-thermostat as described previously.[6] The central lead of the cell was taken to the high-resistance terminal

of the electrometer within a metal tube which provided electrostatic screening. The other lead went to the other terminal of the electrometer and was earthed. After change of temperature, about 30 min. was allowed before measurement at any altered temperature was made; results were reproducible to $\pm 1\%$.

Effects of Decomposition of Complexes.—With these alkali-metal complexes, the resistance of which is much lower than that of the parent hydrocarbons, the slow relaxation effect observed previously [4] (cf. preceding paper) was very little in evidence. Generally, the lower the resistance of the complex the smaller the time required to reach a steady value. With isoviolanthrene complexes no relaxation at all was observed and the final value of resistance was attained at once.

In view of the very low resistances attained as a result of complex formation, it was desirable to verify that the conductivity observed was not due to ions arising from surface decomposition of the complex by water or oxygen. Accordingly, certain pellets were exposed to the air for a few seconds. In every case the electrical behaviour was completely altered. A very marked relaxation effect was then observed on application of the voltage, and the resistance did not reach a steady value for several minutes. Both the resistance and the activation energy of the exposed pellets were increased; when the applied measuring voltage was removed an e.m.f. appeared of opposite polarity to that originally applied. These are the characteristics to be expected from polarisation resulting from ionic conduction. Their absence in the undecomposed complex was taken as a criterion of purity and supports the view that the conductivity of the pure complexes is electronic before decomposition occurs.

Measurement of Thermoelectric Power (T.E.P.).—The cell illustrated in Fig. 3 was used for the measurement of T.E.P. of the alkali-metal complexes. A pelleted sample of the complex was placed in the cell and the two halves, separated by a neoprene O-ring, were clamped together in the same way as in the measurement of conductivity. This again enabled measurements to be made outside the glove box.

The walls of this cell were made of Pyrex glass, which provided sufficient insulation since the highest resistivity of complexes was 10^{11} ohm cm. at room temperature. The electrodes were made of 0·02″ platinum sheet, hard-soldered on to copper cylinders which acted as efficient heat sinks. One of the blocks was hollow and contained a resistance heater wound non-inductively on asbestos insulation. The other block rested on a metal spring to provide firm contacts with the pellet sample. Two leads (0·015″ in diam.) were fused to each platinum metal electrode, one of pure platinum and the other of 87 : 13 platinum–rhodium thermocouple wire. Suitable outside connections enabled the temperature of the electrodes to be measured, with the reference junctions cooled in ice–water. A steady temperature difference was maintained and the thermal e.m.f. across the pellet was measured directly on a Vibron electrometer. Voltages below 1 mv could not be measured accurately, so that fairly large temperature differences were required across the sample to give measurable thermal voltages. For the majority of sodium complexes the T.E.P. was so small that the deflection gave only the sign of the thermal electric current; this was always negative with respect to the cold junction, indicating in these solids that the predominant current carriers are negative.

Where the sample was exposed to the atmosphere for a short period (deliberately or accidentally), the T.E.P. apparently became large and positive with respect to the cold junction. A large standing e.m.f. was produced on the crystal and was obviously due to surface decomposition and polarization of the sample.

The results of conductivity, thermal electric power, and molar volume measurements of the metal aromatic complexes are given in Parts VI [5] and VII,[1] along with results of similar measurements on the pure hydrocarbons and their acceptor complexes.

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977. *Acid-catalysed Ether Fission. Part I. A New Mechanism, in Sulphuric Acid.*

By D. Jaques and J. A. Leisten.

The rates of fission in 99·6% sulphuric acid of 13 alkyl ethers and 4 alkyl aryl ethers have been measured, enabling structural effects on both sides of the breaking bond to be assessed. The variation in rate with the concentration of water and potassium hydrogen sulphate has been studied for two alkyl ethers and one alkyl aryl ether in sulphuric acid containing total solute concentrations of up to 0·3 mole/kg.

The results suggest that alkyl ethers are solvolysed in concentrated sulphuric acid by a previously unsuspected mechanism: the conjugate acid of the ether reacts with sulphur trioxide in a mobile equilibrium to form a complex which, in the rate-determining stage, breaks up into a carbonium ion and an alkyl hydrogen sulphate molecule. The fission of alkyl aryl ethers, however, appears to be a simple A-1 reaction. This difference in mechanism is discussed.

Most ethers are rather resistant to hydrolysis by aqueous acids; and the reaction is not a very easy one to follow by chemical analysis. Consequently there have been few kinetic studies, and there is a dearth of information on which ideas concerning mechanism can be formed.[1] In contrast, much light has been thrown on the hydrolysis of esters and amides by determining, for example, the variation in rate with acid concentration, the effect of substituents in different parts of the molecule, and the dependence of these substituent effects upon the reaction medium.[2] It is hoped in this series to provide some similar information for the hydrolysis (or, more generally, the solvolysis) of ethers, in a wide range of protonic media. The present Part is concerned with the reaction in concentrated sulphuric acid. No kinetic studies have previously been reported.[3]

Results and Discussion

Cryoscopic Results for Aliphatic Ethers in 99·6% Sulphuric Acid.—van't Hoff i-factors of 2·0 to 1·4 (Table 1, col. 4) show that aliphatic ethers ionise as strong or moderately strong bases in 99·6% sulphuric acid: the lower values are reasonably associated with incomplete ionisation according to equation (1), since they are found for the more negatively substituted ethers:

$$RR'O + H_2SO_4 \rightleftharpoons RR'OH^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Solvolysis should lead to approximately four-fold freezing-point depressions, because in this solvent alcohols are converted into alkyl hydrogen sulphates, which behave as non-electrolytes, and water is a strong base:

$$RR'O + 3H_2SO_4 \longrightarrow RHSO_4 + R'HSO_4 + H_3O^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Table 1 summarises the results obtained by following changes in freezing point with time, at temperatures sufficient to cause fission. First-order rate constants (k_1) were calculated by assuming infinity values (i_∞) of the van't Hoff i-factor. The difference between these and the experimentally determined final i-factors (in col. 5) are measures of the reliability of the rate constants. The experimental value is generally a little greater than i_∞ because the products of solvolysis are not completely stable: the products from the butyl ethers are so unstable that the rate constants had to be calculated from initial slopes.

[1] Burwell, *Chem. Rev.*, 1954, **54**, 615.
[2] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953, p. 751.
[3] Gillespie and Leisten, *Quart. Rev.*, 1954, **8**, 51.

Constitutional Effects on the Solvolysis of Aliphatic Ethers.—The relative order of rates shown by results 1—10 in Table 1 can be understood on the basis of three ideas. (i) The rate-determining step is a unimolecular fission of the conjugate acid [equation (3)] or of some other complex formed from the solvent and the ether:

. . . . . (3)

(ii) Fission occurs so as to produce the more stable carbonium ion; and this decides which of the two carbon–oxygen bonds will break. (iii) Constitutional effects are greater in the potential carbonium ion than in the remote branch of the ether, but positive or negative inductive effects in the remote branch respectively retard or accelerate the heterolysis.

To apply these principles it is first necessary to decide for each ether which branch can form the more stable carbonium ion. We have taken the order to be: $Pr^i > Bu^n >$ Et > 2-chloroethyl > 2-sulphatoethyl > Me. The first part of the series is straightforward; 2-chloroethyl follows ethyl because the inductive effect of the chlorine atom opposes the dispersal of positive charge; and 2-sulphatoethyl comes later still because the sulphato-group is more strongly electron-attracting than chlorine. On the basis of inductive effects methyl should lie between ethyl and 2-chloroethyl, but for the rather similar heterolysis of acetals and ketals Kreevoy and Taft [4] have shown the importance of hyperconjugation by β-hydrogen atoms: since 2-chloroethyl and 2-sulphatoethyl each have two β-hydrogen atoms to stabilise the carbonium ion and methyl has none it is at least defensible to place methyl last in the series. In Table 1 the groups which should separate as carbonium ions on the basis of this series are designated R, and in order to provide comparable figures (k') for the rate of fission at one carbon–oxygen bond the rate constants for symmetrical ethers have been halved. Ethers 1—5 have the same group R′, and the importance of constitutional effects in R is shown by the large differences required to bring about reaction at a convenient rate (from 25° for methyl n-butyl ether to 90° for methyl ether): the order of rates follows the stability series.

TABLE 1.

Cryoscopic results for aliphatic ethers (RR′O) in 99·6% sulphuric acid.

No.	R	R′	Initial *i*-factor	Final *i*-factor	i_∞	Reaction temp.	10^3k_1 (min.$^{-1}$)	k'
1 *	Me	Me	1·80	4·38	4·05	90·0°	3·41	1·70
2 †	$CH_2{\cdot}CH_2{\cdot}SO_4H$	Me	1·4	3·7	4·0	65·0	1·69	1·69
3	$CH_2{\cdot}CH_2Cl$	Me	1·79	4·28	4·15	65·0	3·4 ‡	3·4
4 *	Et	Me	1·90	—	4·11	55·0	13·8	13·8
5	Bu^n	Me	1·93	—	—	25·0	16	16
6	Et	Et	2·00	4·42	4·25	55·0	6·93	3·46
7	Et	$CH_2{\cdot}CH_2Cl$	1·95	—	4·10	55·0	18·8	18·8
8 †	Et	$CH_2{\cdot}CH_2{\cdot}SO_4H$	1·6	—	4·0	55·0	24·2	24·2
9	Bu^n	Bu^n	2·04	—	—	25·0	6	3
10	Pr^i	Pr^i	2·24	4·38	4·25	25·0	40	20
11	$CH_2{\cdot}CH_2Cl$	$CH_2{\cdot}CH_2Cl$	1·56	4·54	4·45	65·0	4·96	2·49
12	$CH_2{\cdot}CH_2Br$	Me	1·82	3·66	3·65	25·8	27·2	27·2
13	$CH_2{\cdot}CH_2Br$	Et	2·02	—	4·00	25·8	4·90	4·90

* For these volatile ethers the *i*-factors in cols. 4, 5, and 6 are in the correct ratios, but the absolute magnitudes are uncertain.

† The sulphato-ethers were prepared *in situ* from corresponding hydroxy-ethers, a process which produces water. The *i*-factor for water (1·9) has been subtracted from the observed values.

‡ Derived from a measurement at 70·0° ($k = 5{\cdot}8 \times 10^{-3}$) by assuming an activation energy of 25 kcal./mole. (This value was found for 2-chloroethyl ethyl ether from measurements in 99·6% H_2SO_4 at four temperatures.)

The effect of substituents in the remote branch, R′, should be purely inductive, and for ethers with the same group R the rate should decrease in the following order of groups R′, without ambiguity: 2-sulphatoethyl > 2-chloroethyl > Me > Et. Ethers 6, 4, 7, and 8

[4] Kreevoy and Taft, *J. Amer. Chem. Soc.*, 1955, **77**, 5590.

constitute such a series (R = ethyl). The order of rates is that predicted, and the effects are sufficiently small that the whole series can be studied at the same temperature.

Of the remaining ethers di-n-butyl ether reacts more slowly than n-butyl methyl ether as expected, and di-isopropyl ether reacts the fastest of the whole series. Comparison of the results for di-(2-chloroethyl) ether and 2-chloroethyl methyl ether reveals a small anomaly which might be ascribed to a second-order effect, such as the difference in basicity (see Table 1, col. 4). The bromo-ethers on the other hand depart seriously from their predicted behaviour. The Taft σ^* values for chloromethyl and bromomethyl (+1·050 and +1·030) are such that no detectable difference in rate would be forecast for corresponding chloro- and bromo-ethers. In fact, however, the bromo-ethers are much more reactive, and in contrast to the corresponding chloro-ethers 2-bromoethyl methyl ether is cleaved more easily than 2-bromoethyl ethyl ether. Ethyl 2-iodoethyl ether was found to liberate iodine immediately on dissolution. This raises the interesting possibility for the bromo-ethers that some interaction with solvent occurs which greatly modifies the polar character of the bromine atom without actually causing it to separate. These observations clearly require a special explanation: the results in general support our assumption of a rate-determining unimolecular dissociation, and we next consider the nature of the dissociating species.

TABLE 2.

Rates of solvolysis of aliphatic ethers in sulphuric acid containing hydroxonium, potassium, or ammonium hydrogen sulphate.

Diethyl ether at 45·0°.					Di-2-chloroethyl ethyl ether at 39·0°.				
Molality				10^5k_1	Molality				10^5k_1
Water	$KHSO_4$	Ether	HSO_4^- *	(min.$^{-1}$)	Water	$KHSO_4$	Ether	HSO_4^- *	(min.$^{-1}$)
0·214		0·033	0·247	2·17	0·230		0·052	0·282	2·64
0·153		0·033	0·186	3·50	0·190		0·052	0·242	4·12
0·074		0·049	0·124	8·13	0·130		0·052	0·182	6·67
0·072		0·044	0·117	8·29	0·064		0·052	0·117	16·0
0·072		0·029	0·103	10·4	0·051		0·057	0·109	22·5
0·074		0·025	0·101	11·1	0·037		0·054	0·093	31·9
0·036		0·022	0·062	25·6	0·000		0·053	0·057	59·8
0·000		0·063	0·067	27·4	0·000		0·071	0·074	41·0
0·000	0·186	0·044	0·230	14·5	0·000	0·145	0·053	0·198	26·1
					0·000	0·193	0·052	0·245	23·7
					0·000	0·241	0·054	0·295	20·1
					0·000	0·086 †	0·056	0·142	35·4

* The sum of the molalities of water, potassium hydrogen sulphate, and ether, with a small correction (maximum 0·004) for the self-dissociation of the solvent (Bass, Gillespie, and Robinson, *J.*, 1960, 821).

† Ammonium hydrogen sulphate.

Variation of Rate with Acid Composition for Aliphatic Ethers.—Rate constants for the solvolysis of ethyl ether and 2-chloroethyl ethyl ether in solutions containing different amounts of water (hydroxonium hydrogen sulphate) and of potassium and ammonium hydrogen sulphate are given in Table 2; and the important features are displayed in Fig. 1. It is clear that in concentrated sulphuric acid the rate of fission of alkyl ethers is very sensitive to hydrogen sulphate concentration, but that it is much more sensitive to hydroxonium hydrogen sulphate (line A) than other hydrogen sulphates (line B). (These solutions contain a significant amount of hydrogen sulphate ion derived from the basic ionisation of the ethers, and the points which define line A actually show the combined effects of large variations in water concentration and small variations in the concentration of hydrogen sulphate ion from the ether. The present results, however, are insufficiently precise to enable us to separate the small effect of the ether from the large effect of water, and for this reason and to simplify discussion we shall refer to these results as though they show the effect of water alone on the rate of fission.)

Since aliphatic ethers exist predominantly as conjugate acid in these solutions the

relative concentration of conjugate acid can vary little from one solution to another, and if this were the species undergoing fission the points in Fig. 1 would lie on a horizontal straight line. Suppose next that the doubly protonated ether were the reactive intermediate: by equation (4) the rate would be inversely proportional to the hydrogen sulphate concentration, and Fig. 1 would show a single straight line of unit negative slope.

$$RR'OH^+ + H_2SO_4 \rightleftharpoons RR'OH_2^{++} + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

In seeking other explanations for the observed pattern we noticed a similarity between our results and those obtained by Cowdrey and Davies for aromatic sulphonation in 92—99% sulphuric acid.[5] We therefore carried out experiments in sulphonation in similar solutions to those used in the ether solvolyses and using the same cryoscopic technique. The results (Fig. 2) show definite similarity to those for ether fission, the

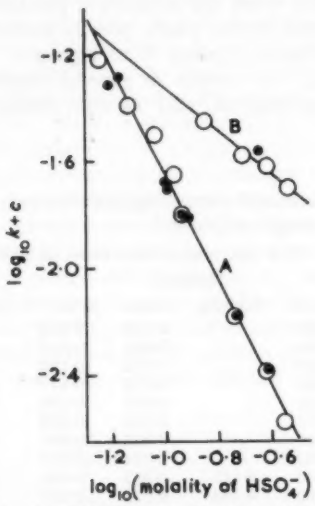

FIG. 1. Effect of hydrogen sulphate concentration on the solvolysis of aliphatic ethers in sulphuric acid.

○ Di-2-chloroethyl ether at 39·0° (c = 0·00).
● Diethyl ether at 45·0° (c = 0·32).
A, hydroxonium hydrogen sulphate.
B, potassium or ammonium hydrogen sulphate.

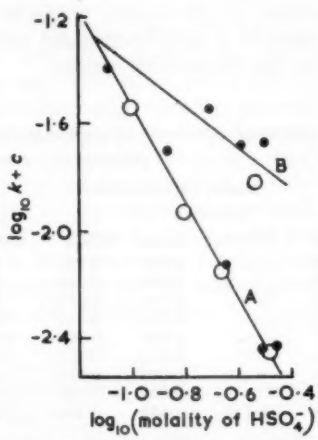

FIG. 2. Effect of hydrogen sulphate concentration on the rate of sulphonation in sulphuric acid.

○ *p*-Nitrotoluene at 96·5° (c = 0·05).
● Benzylideneacetone at 54·8° (c = 0·00).
A, hydroxonium hydrogen sulphate.
B, potassium hydrogen sulphate.

solutions containing water being associated with sharper rate-dependence than the potassium hydrogen sulphate solutions. Results of this type [5] can be understood if the sulphonating agent is sulphur trioxide (or one of its solvates [6]) for the rate should then be proportional to the concentration of sulphur trioxide formed by dissociation of the solvent, and this dissociation is suppressed more sharply by hydroxonium sulphate than by other hydrogen sulphates:

$$2H_2SO_4 \rightleftharpoons SO_3 + HSO_4^- + H_3O^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The same assumption, that the rate is proportional to the concentration of sulphur trioxide, is equally successful in explaining our results on ether fission. If the variations

[5] Cowdrey and Davies, *J.*, 1949, 1871.
[6] Ref. 2, p. 300.

in rate are controlled by dissociation (5) the lines in Figs. 1 and 2 for aqueous solutions should have slopes of −2, and the other lines slopes of −1: the observed slopes for sulphonation are −1·80 and −0·77 (±0·4), and for ether fission −2·02 and −0·81. The results for sulphonation show greater experimental scatter than those for solvolysis, and they have a limitation similar to that described for the ether results in that the aromatic substrate and the solvent produce a significant concentration of hydrogen sulphate ions. The similar sensitivity of these two reactions to the composition of the solvent is nevertheless apparent, and it is difficult to ascribe it to any factor other than the concentration of sulphur trioxide.

The Mechanism of Solvolysis for Aliphatic Ethers.—In concentrated sulphuric acid ether fission appears to be a unimolecular process, but the overall rate is proportional to the concentration of sulphur trioxide. To reconcile these conclusions we propose a two-step mechanism: a pre-equilibrium (6) which accounts for the solvent effects, and a heterolysis (7) on which the observed constitutional effects depend:

$$RR'OH^+ + SO_3 \rightleftharpoons RR'SO_4H^+ \quad (6)$$

$$R\text{—}\overset{\curvearrowright}{O}^+\text{—}R' \longrightarrow R^+ + R'HSO_4 \quad (7)$$
$$\quad\quad\quad

there are significant differences between the two series, for initial i-factors (Table 3, col. 3) show that the alkyl aryl ethers are weak bases in sulphuric acid, and the i-values show a tendency for the aryl group to remain in solution as a phenol rather than as the phenyl

TABLE 3.

Cryoscopic results for alkyl aryl ethers in 99·6% sulphuric acid.

R	R′	Initial i-factor	Final i-factor	i_∞	Reaction temp.	10^3k_1
Me	2,4-$(NO_2)_2C_6H_3$	1·23	3·24	3·0	85·0°	32·1
Me	3,5-$(NO_2)_2C_6H_3$	1·14	3·34	3·0	85·0	9·16
Et	2,4-$(NO_2)_2C_6H_3$	1·29	2·45	2·4	25·6	38·7
Et	2-Me-5-NO_2·C_6H_3	1·36	—	4·0	25·6	12·1

hydrogen sulphate. If the phenol produced in the fission of an alkyl aryl ether behaves as a non-electrolyte the final i-factor should be approximately 2:

$$RR'O + H_2SO_4 \rightleftharpoons RHSO_4 + R'OH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

In fact 2,4-dinitrophenol is about one-third ionised as a base in 100% sulphuric acid,[8] and so the final i-value in the fission of alkyl 2,4-dinitrophenyl ethers should be about 2·3,

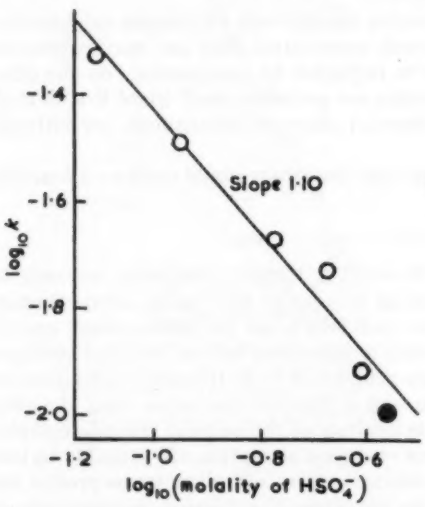

FIG. 3. Effect of hydrogen sulphate concentration on the solvolysis of 2-methyl-5-nitrophenetole in sulphuric acid.

○ Aqueous sulphuric acid.
● Sulphuric acid containing $KHSO_4$.

in good agreement with the observed results for 2,4-dinitrophenetole. The high value of i_∞ (3·0) for both 2,4- and 3,5-dinitroanisole suggests side reactions, which are not unexpected in this solvent at 85°, but the still higher value (of 4·0) for the solvolysis of 2-methyl-5-nitrophenetole at 25° shows that the phenol forms a hydrogen sulphate, a conclusion which might be predicted from the similar behaviour of *m*-nitrophenol.[8]

The rationale for the sulphur trioxide mechanism depends on a much greater stability in sulphuric acid of an alkyl hydrogen sulphate than the corresponding alcohol. Facts presented above suggest that the difference in stability between phenols and their hydrogen sulphates is small, since a relatively small change in the substituents can swing the equilibrium (8) from one side to the other. We should therefore be prepared for alkyl

[7] Bass, Gillespie, and Robinson, *J.*, 1960, 821.
[8] Gillespie and Oubridge, *J.*, 1959, 2804.

aryl ethers to be solvolysed by a different mechanism, and results for 2,4-dinitrophenetole in Table 4 show that this is certainly the case. Suppose that the conjugate acid were

TABLE 4.

Rates of solvolysis of alkyl aryl ethers in sulphuric acid containing hydroxonium and potassium hydrogen sulphates.

2-Methyl-5-nitrophenetole at 25·6°.					2,4-Dinitrophenetole at 25·6°.				
Molality				10^3k_1	Molality				10^3k_1
Water	$KHSO_4$	Ether	HSO_4^- *	(min.$^{-1}$)	Water	$KHSO_4$	Ether	HSO_4^- *	(min.$^{-1}$)
0·220		0·053	0·246	12·1	0·220		0·052	0·246	38·7
0·186		0·052	0·212	18·5	0·058	0·159	0·052	0·243	40·9
0·142		0·053	0·168	21·2					
0·084		0·052	0·111	32·1					
0·049		0·052	0·077	47·0					
0·058	0·204	0·031	0·277	9·90					

* The sum of the molalities of water and potassium hydrogen sulphate, plus half the molality of the ether.

the species which undergoes heterolysis: its concentration should vary inversely with the hydrogen sulphate ion concentration according to equation (9) regardless of whether the

$$RR'O + H_2SO_4 \rightleftharpoons RR'OH^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

hydrogen sulphate ion is derived from water or potassium hydrogen sulphate. The single line of nearly unit negative slope in Fig. 3 is consistent with this mechanism for 2-methyl-5-nitrophenetole, and the apparent insensitivity to hydroxonium ion of the rate of fission of 2,4-dinitrophenetole (Table 4) suggests the same conclusion for this ether. The prevalence of a different mechanism for these ethers provides interesting support for our interpretation of the solvolysis of alkyl ethers in the same solvent.

EXPERIMENTAL

Cryoscopic Measurements.—The measurements of *i*-factors and of rate constants were carried out as in previous work.[9] The concentration of water in the solvent was determined by reference to the freezing point. Potassium and ammonium hydrogen sulphate were added as the normal sulphates.

Product Analysis.—Proof of the solvolysis of ethyl ether was obtained by hydrolysing the ethyl hydrogen sulphate and then estimating the ethyl alcohol by volumetric oxidation. The procedure has been used for determining the rate of fission in other media and will be described fully in a later Part. Solutions in which bromo- and chloro-ethers had been solvolysed all gave negative tests for halide ions. Proof of fission was obtained for alkyl aryl ethers by diluting the reaction mixtures so as to precipitate phenols which were then purified and identified.

Materials.—A number of the ethers were obtained commercially, and the preparations of all the remainder have been previously described. Reasonable care was taken in purifying and testing for purity: *e.g.*, all liquids were dried and fractionated. Satisfactory analyses were obtained for the bromo-ether.

CHEMISTRY DEPARTMENT, UNIVERSITY OF SHEFFIELD. [*Received, June 7th,* 1961.]

[9] Leisten, *J.*, 1956, 1572.

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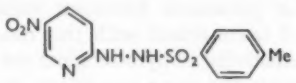
978. *Some Unusual Reactions of Toluene-*p*-sulphonhydrazide.*

By A. Deavin and C. W. Rees.

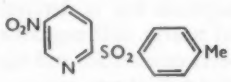
Toluene-*p*-sulphonhydrazide reacts with 2-chloro-5-nitropyridine in hot ethanol to give, not the expected hydrazino-compound (I), but the sulphone (II); the mechanism of the reaction is discussed. Products of decomposition of toluene-*p*-sulphonhydrazide in boiling ethanol are identified.

Toluene-*p*-sulphonhydrazidium toluene-*p*-sulphonate (VI) is shown to be the product obtained by Hälssig by heating toluene-*p*-sulphinic acid with hydrazine hydrochloride.

A convenient method for the removal of a reactive halogen atom from heterocyclic compounds containing other easily reduced groups is reaction with toluene-*p*-sulphonhydrazide followed by alkaline decomposition of the product.[1-3] When this method was applied to the preparation of 3-nitropyridine from 2-chloro-5-nitropyridine an anomalous reaction occurred. 2-Chloro-5-nitropyridine and toluene-*p*-sulphonhydrazide in chloroform or ethanol kept at room temperature for up to two weeks gave none of the expected 5-nitro-2-toluene-*p*-sulphonhydrazidopyridine (I), and only traces were formed on heating the ethanolic solution. The pyridine-containing product was 5-nitro-2-toluene-*p*-sulphonylpyridine (II). The pyridylhydrazide (I) was prepared from 2-hydrazino-5-nitropyridine and toluene-*p*-sulphonyl chloride; it did not yield the sulphone (II) in boiling ethanol even when toluene-*p*-sulphonhydrazide and hydrochloric acid were added



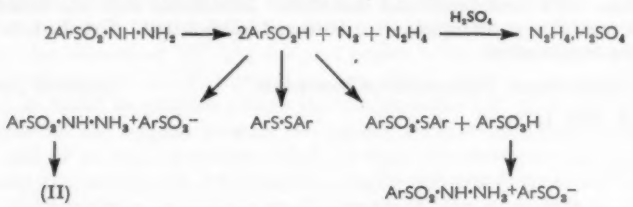
(I)



(II)

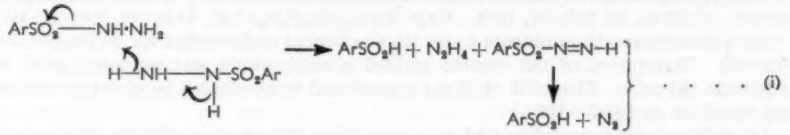
to simulate the conditions under which the sulphone was obtained. Under these conditions *p*-tolyl toluene-*p*-thiolsulphonate was isolated, and this was also formed, together with di-*p*-tolyl disulphide, from toluene-*p*-sulphonhydrazide and ethanolic hydrochloric acid, when the pyridylhydrazide (I) was omitted. When toluene-*p*-sulphonhydrazide was heated alone in ethanol the toluene-*p*-thiolsulphonate was not formed but the disulphide was obtained, together with toluene-*p*-sulphinic acid, toluene-*p*-sulphonhydrazidium toluene-*p*-sulphinate and toluene-*p*-sulphonate. The toluene-*p*-thiolsulphonate was also not detected when the hydrochloric acid was replaced by small amounts of water or sulphuric acid. In the presence of the latter the other products mentioned above were formed together with hydrazine sulphate. Benzenesulphonhydrazide has been reported [4] to yield 1,2-dibenzenesulphonylhydrazine when heated in ethanol, but none of the corresponding ditoluenesulphonyl compound was found in our reactions.

The annexed scheme summarises the likely routes to the compounds isolated when toluene-*p*-sulphonhydrazide ($ArSO_2{\cdot}NH{\cdot}NH_2$) decomposes in ethanol:



[1] Dewar, *J.*, 1944, 619.
[2] Albert and Royer, *J.*, 1949, 1148.
[3] Alford and Schofield, *J.*, 1953, 609.
[4] Curtius and Lorenzen, *J. prakt. Chem.*, 1898, **58**, 166.

Formation of the sulphinic acid involves reduction of the hydrazides; the initial reducing agent must be another hydrazide molecule, as shown in (i). Sulphonhydrazides are known to reduce ammoniacal silver nitrate, Fehling's solution and mercuric oxide.[4] The hydrazine formed could then act catalytically as a reducing agent (cf. ref. 5).



Curtius and Haas [6] showed that benzylsulphonhydrazide decomposed in boiling water or ethanol to form benzylsulphinic acid and, following Raschig,[7] they claimed that nitrogen and hydrogen were evolved:

$$PhCH_2{\cdot}SO_2{\cdot}NH{\cdot}NH_2 \longrightarrow PhCH_2{\cdot}SO_2H + N_2 + H_2$$

However, from the decomposition in ethanol they isolated hydrazinium benzyl sulphonate and, furthermore, the volume of gas liberated corresponded exactly to the formation of one mole of gas from two moles of hydrazide [see equation (i)] rather than the reverse, which their equation requires.

Formation of the other decomposition products follows readily from the presence of toluene-*p*-sulphinic acid, which would be expected to disproportionate [8] to a mixture of *p*-tolyl toluene-*p*-thiolsulphonate and toluene-*p*-sulphonic acid and to react, as the anion, with 2-chloro-5-nitropyridine to form the sulphone (II). Indeed, heating an ethanolic solution of 2-chloro-5-nitropyridine and sodium-*p*-toluenesulphinate rapidly gave this sulphone in good yield. Finally, the disulphide could be formed by reduction of the sulphinic acid or thiolsulphonate by the hydrazine liberated. Curtius and Lorenzen [4] isolated diphenyl disulphide by heating benzenesulphonhydrazide alone above its melting-point.

By heating toluene-*p*-sulphinic acid with aqueous hydrazine hydrochloride Hälssig [9] obtained *p*-tolyl toluene-*p*-thiolsulphonate and a crystalline compound, $C_{14}H_{18}N_2O_5S_2$, m. p. 180·5°, which was insoluble in organic solvents but soluble in water to give an acid solution which reduced ammoniacal silver nitrate, and which gave a benzoyl derivative, m. p. 209·5°. This compound is now shown to be toluene-*p*-sulphonhydrazidium toluene-*p*-sulphonate; and the benzoyl derivative is the dibenzoyl derivative of toluene-*p*-sulphonhydrazide. The salt is presumably formed by disproportionation of the sulphinic acid to the thiolsulphonate and the sulphonic acid, reaction of the latter with hydrazine to form toluene-*p*-sulphonhydrazide, and combination of this with excess of sulphonic acid.

Experimental

*5-Nitro-2-toluene-*p*-sulphonhydrazidopyridine* (I).—Toluene-*p*-sulphonyl chloride (8·3 g.) in pyridine (20 ml.) was added to 2-hydrazino-5-nitropyridine [10] (7 g.) in pyridine (450 ml.), and set aside for 2 days. Water (1 l.) was added and the precipitate (4·5 g.) crystallised from acetic acid or ethanol, giving the *hydrazide*, m. p. 214° (decomp.) (Found: C, 46·6; H, 4·3; N, 18·1. $C_{12}H_{12}N_4O_4S$ requires C, 46·8; H, 3·9; N, 18·2%).

*5-Nitro-2-toluene-*p*-sulphonylpyridine* (II).—(*a*) Condensation of 2-chloro-5-nitropyridine with *p*-thiocresol and oxidation of the sulphide by Passerini's method [11] gave the sulphone, m. p. 159·5—160·5° after three recrystallisations from ethanol.

(*b*) Toluene-*p*-sulphonhydrazide [2] (3·85 g.) in ethanol (50 ml.) and 2-chloro-5-nitropyridine (1·38 g.) in ethanol (75 ml.) were mixed. 5-Nitro-2-toluene-*p*-sulphonhydrazidopyridine (I) did not separate on storage at room temperature for 20 hr. or after the solution had been

[5] Dunn and Davies, *J.*, 1929, 1050.
[6] Curtius and Haas, *J. prakt. Chem.*, 1921, **102**, 85.
[7] Raschig, *Z. angew. Chem.*, 1913, **26**, III, 134.
[8] Bredereck, Wagner, Beck, Herlinger, and Kottenhann, *Angew. Chem.*, 1958, **70**, 268.
[9] Hälssig, *J. prakt. Chem.*, 1897, **56**, 222.
[10] Brown, *J. Amer. Chem. Soc.*, 1954, **76**, 3167.
[11] Passerini, *Boll. sci. Fac. Chim. ind. Bologna*, 1951, **9**, 1, 31; *Chem. Abs.*, 1951, **45**, 10,210.

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refluxed for a further 3 hr., though the presence of a very small amount was indicated by the red colour produced by addition of aqueous sodium hydroxide. (It was also found that only a trace of the hydrazide was formed on storage of the reaction mixture, in ethanol or chloroform, for up to 2 weeks.) The volume of the solution was reduced to one half and the sulphone (II) was separated; after recrystallisation from ethanol this had m. p. and mixed m. p. 160—161° (Found: C, 52·4; H, 3·7; N, 10·3. Calc. for $C_{12}H_{10}N_2O_4S$: C, 51·8; H, 3·6; N, 10·1%).

(*c*) The same reaction mixture as for (*b*) was heated under reflux for 50 hr. and the ethanol removed. Trituration of the residue yielded a solid which was extracted with 2N-sodium hydroxide (40 ml.). The solid (1·75 g.) crystallised from ethanol to give the sulphone, m. p. and mixed m. p. 159·5—160°.

(*d*) 2-Chloro-5-nitropyridine (0·3 g.) and sodium toluene-*p*-sulphinate dihydrate [12] (0·4 g.) in ethanol (25 ml.) were heated under reflux for 1·5 hr.; sodium chloride separated. More sulphinate (0·4 g.) was added and heating continued for a further 1 hr. The volume was reduced to 10 ml. and water (15 ml.) was added with stirring, whereupon the sulphone (0·3 g.), m. p. and mixed m. p. 158—160°, separated.

Stability of 5-*Nitro*-2-*toluene*-p-*sulphonhydrazidopyridine* (I) *in Boiling Ethanol.*—(*a*) The hydrazide (I) (1·5 g.) in ethanol (50 ml.) was heated under reflux for 60 hr. On cooling, starting material (0·52 g.), m. p. 213—214°, was collected and more (0·1 g.) was obtained on removal of the solvent.

(*b*) The hydrazide (I) (1·0 g.) was suspended in ethanol (40 ml.) containing 5·5N-aqueous hydrochloric acid (0·3 ml.) and heated under reflux for 18 hr. After cooling, starting material (0·82 g.), m. p. 214—215°, was recovered.

(*c*) The hydrazide (I) (0·70 g.) and toluene-*p*-sulphonhydrazide (0·98 g.) in ethanol (30 ml.) containing 5·5N-aqueous hydrochloric acid (2·2 ml.) were heated under reflux for 23 hr. From the cooled solution unchanged hydrazide (I) (0·36 g.) was obtained. Removal of the ethanol and extraction of the residue with 2N-sodium hydroxide left a solid (0·3 g.) which, after two recrystallisations from ethanol, gave *p*-tolyl toluene-*p*-thiolsulphonate (III), m. p. and mixed m. p. with authentic material [13] 76—78°.

Thermal Decomposition of Toluene-p-*sulphonhydrazide in Ethanol.*—(*a*) *Alkali-insoluble products.* Toluene-*p*-sulphonhydrazide (3·85 g.) in ethanol (120 ml.) containing concentrated hydrochloric acid (0·28 g.) was heated under reflux for 72 hr. The ethanol was removed and the residue (3·5 g.) was extracted with 2N-sodium hydroxide (15 ml.) to leave an insoluble solid (0·63 g.), m. p. 30—75°, separated by light petroleum (b. p. 40—60°) into the soluble di-*p*-tolyl disulphide (0·34 g.), m. p. and mixed m. p. with authentic material [14] 39—42°, and the insoluble *p*-tolyl toluene-*p*-thiolsulphonate (0·24 g.), m. p. and mixed m. p. 68—72°. In similar reactions, but with the hydrochloric acid omitted or replaced by sulphuric acid or by water, the ester was not detected but the disulphide was isolated in yields of up to 40%. In the presence of sulphuric acid, hydrazine sulphate, m. p. and mixed m. p. 251°, separated from the ethanolic solution.

(*b*) *Alkali-soluble products.* The sodium hydroxide extracts from the decompositions described in (*a*) were acidified with 4N-hydrochloric acid, and a typical isolation procedure was as follows. The precipitate (0·62 g.) crystallised from water to give toluene-*p*-sulphinic acid, m. p. and mixed m. p. with an authentic specimen [13] (87·5—88·5° (Found: C, 53·5; H, 5·2; S, 20·7. Calc. for $C_7H_8O_2S$: C, 53·8; H, 5·2; S, 20·5%). This compound gave an orange precipitate with ferric chloride solution and a deep purple-blue colour in concentrated sulphuric acid with anisole (Smiles's test). On storage, the acid mother liquor deposited crystals which recrystallised from ethanol to give *toluene*-p-*sulphonhydrazidium toluene*-p-*sulphonate* (0·1 g.), m. p. and mixed m. p. with a sample prepared as described later, 178·5—180° (decomp.) (Found: C, 46·8; H, 5·0; S, 17·3. $C_{14}H_{18}N_2O_5S_2$ requires C, 46·9; H, 5·1; S, 17·8%). In another experiment on storage of this acid mother liquor a crystalline solid (0·13 g.) separated which melted with resolidification at 95—100° and finally melted at 169—173°. Since heating this solid at 100—150° converted it into toluene-*p*-sulphonhydrazidium toluene-*p*-sulphonate, m. p. and mixed m. p. 172—175°, it was considered to be *toluene*-p-*sulphonhydrazidium toluene*-p-*sulphinate* (Found: C, 48·8; H, 5·0. $C_{14}H_{18}N_2O_4S_2$ requires C, 49·1; H, 5·3%). Its initial m. p., 95°, was undepressed on admixture with a sample prepared as described below.

[12] Whitmore and Hamilton, *Org. Synth.*, Coll. Vol. I, 492.
[13] Smiles, *J.*, 1924, **125**, 180.
[14] Field and Grunwald, *J. Org. Chem.*, 1951, **16**, 952.

*Toluene-*p*-sulphonhydrazidium Toluene-*p*-sulphonate.*—Toluene-*p*-sulphonhydrazide (1·7 g.) suspended in water (20 ml.) was just dissolved by addition of concentrated hydrochloric acid, and toluene-*p*-sulphonic acid hydrate (2 g.) in water (5 ml.) was added. The precipitate was crystallised from ethanol to give the salt, m. p. 179—180° (decomp.).

*Toluene-*p*-sulphonhydrazidium Toluene-*p*-sulphinate*—Toluene-*p*-sulphinic acid (0·04 g.) in 2N-sodium hydroxide (0·5 ml.) and toluene-*p*-sulphonhydrazide (0·05 g.) in 2N-hydrochloric acid (1 ml.) were mixed, and the white crystalline mass was collected and washed with water. It melted with resolidification at 90—95°, finally melting at 169—175°.

*Reaction between Toluene-*p*-sulphinic Acid and Hydrazine Hydrochloride.*—Cf. Hälssig.[9] Toluene-*p*-sulphinic acid (0·73 g.) was added to hydrazine hydrochloride (0·32 g.) in water (6·5 ml.) containing 5·5N-hydrochloric acid (0·16 ml.), and the mixture was gently heated and then boiled for 1 hr. The precipitated oil solidified to give *p*-tolyl toluene-*p*-thiolsulphonate (0·25 g.), m. p. and mixed m. p. 76—78°, when the solution cooled. The crystals (0·03 g.), formed throughout the mother-liquor, were collected, washed with ether, and shown by mixed m. p. and identity of the infrared spectra (Nujol mull) to be toluene-*p*-sulphonhydrazidium toluene-*p*-sulphonate. A higher yield (0·17 g.) was obtained if the mother-liquor was stored overnight.

Benzoylation of the salt or of toluene-*p*-sulphonhydrazide by the Schotten–Baumann method yielded the *dibenzoyl* derivative of the latter, with variable melting-point, between 206° and 235°, depending on the rate of heating (Found: C, 64·2; H, 5·0; N, 6·9. $C_{21}H_{18}N_2O_4S$ requires C, 64·0; H, 4·6; N, 7·1%). Hälssig reports [9] m. p. 209·5°.

Grateful acknowledgment is made to the Department of Scientific and Industrial Research for a Studentship to A. D.

King's College (University of London),
Strand, London, W.C.2.

[*Received, June 20th*, 1961.]

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979. *Mechanism of the Addition of Trifluoroiodomethane to Ethylene.*

By T. N. Bell.

The thermal reaction between trifluoroiodomethane and ethylene yields addition products $CF_3{\cdot}[CH_2{\cdot}CH_2]_n{\cdot}I$; the main product being 1,1,1-trifluoro-3-iodopropane ($n = 1$). The rate of the addition is given by two limiting rate equations which arise from two propagating steps, each of which can be made rate-controlling depending on the reactant ratio CF_3I/C_2H_4. A mechanism is suggested which satisfactorily accounts for the dependence of the rate of addition on the reactant concentration.

The thermally or photochemically initiated reaction in which trifluoroiodomethane adds to olefins has been used to prepare fluoroalkyl derivatives.[1] In the present case 1,1,1-trifluoro-3-iodopropane is the main product; however, at low trifluoroiodomethane : ethylene ratios some telomers $CF_3{\cdot}[C_2H_4]_n{\cdot}I$, where $n > 1$, are formed. As these additions have only been investigated qualitatively it was decided to study kinetically the reaction between trifluoroiodomethane and ethylene with a view to establishing the mechanism.

Experimental

Materials.—Ethylene was obtained from a cylinder (C.I.G. brand) and purified by fractionation through traps cooled to −72°, −95°, −129°, and liquid-air temperature. The fraction collecting in liquid air was shown to contain no detectable impurity (by molecular weight determination and gas chromatography).

Trifluoroiodomethane was prepared by heating silver trifluoroacetate with iodine.[2] The

[1] Haszeldine, *J.*, 1949, 2856; 1953, 3761.
[2] Haszeldine, *J.*, 1951, 584.

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impure gas was washed with sodium hydroxide solution and dried (P_2O_5), then fractionated as above. The fraction collected at −129° contained no detectable impurity (molecular weight determination and gas chromatography). The purified product was stored at liquid-air temperature.

Apparatus.—A conventional static high-vacuum apparatus was used. The Pyrex-glass vessel (81 ml.) was fitted with a thermocouple well, and was embedded in a tubular furnace, the temperature being controlled to within 0·5° with a Sunvic RT2 temperature controller. Pressures were measured with a constant-volume manometer similar to that described by Dodd and Robinson;[3] this was modified by using air pressure and suction to raise and lower the mercury in the manometer limbs, thereby eliminating a manually operated mercury reservoir connected by rubber tubing, and preventing contamination of the mercury. The modified manometer is shown in Fig. 1. Pressure readings were obtained by using two cathetometers, focused on the manometer limbs.

It was found impossible to make and store mixtures of the two gases, as reaction was initiated in the mixing vessel by sun and fluorescent light. The two gases were therefore

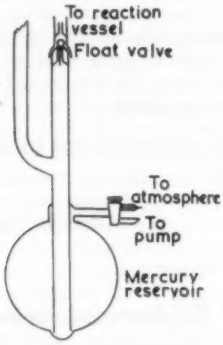

FIG. 1. Constant-volume manometer.

admitted separately to the vessel through a two-way capillary tap, the time interval between successive additions being less than 5 sec.

The stoicheiometry of the reaction was determined by use of gas chromatography (Perkin-Elmer model 154 C). The procedure adopted was to empty the contents of the vessel after a given heating time through a trap cooled to −78° in order to removal all products; the residual starting materials were then condensed into a liquid-air trap. This trap, of standard volume, was then warmed to 20° and attached to the gas-sampling device on the gas chromatograph where the contents were equilibrated with a standard 1-ml. sampling volume; the total pressure could be read on a manometer incorporated in the system. Separation was achieved on a 2-m. column containing di-isodecyl phthalate as the liquid phase, and the partial pressure of each component was determined from the recorded peaks.

The kinetics of the reaction were followed by measuring the rate of change of pressure with time; initial rates were determined from the pressure–time curves.

RESULTS

Stoicheiometry.—A number of runs at 309° with the same initial reactant composition but different heating times were analysed for residual trifluoroiodomethane and ethylene by gas chromatography. The process was repeated for several series of runs, each series differing in the trifluoroiodomethane : ethylene ratio. At pressure ratio trifluoroiodomethane : ethylene = 1·9 and 3·0, corresponding to total reactant pressures of 135 and 172 mm., the rate of consumption of ethylene and trifluoroiodomethane was the same. When the pressure ratio was reduced to 1·3 at a total pressure of 107 mm. the amount of ethylene consumed was slightly greater than the amount of trifluoroiodomethane consumed. It being assumed that the excess of ethylene was used in the formation of a dimer adduct the increased consumption of ethylene corresponded to 5% of telomer in the total product.

[3] Dodd and Robinson, " Experimental Inorganic Chemistry," Elsevier, Amsterdam, 1954, p. 122.

The stoicheiometry can then be expressed by equations (*a*) and (*b*).

$$CF_3I + C_2H_4 \longrightarrow CF_3{\cdot}CH_2{\cdot}CH_2I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (a)$$

$$CF_3I + nC_2H_4 \longrightarrow CF_3{\cdot}[C_2H_4]_n{\cdot}I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b)$$

At reactant ratios $CF_3I/C_2H_4 > 1{\cdot}9$, eqn. (*a*) may be considered to be solely operative, while below this ratio both eqns. (*a*) and (*b*) are operative, the extent of eqn. (*b*) increasing with a decreasing trifluoroiodomethane : ethylene ratio.

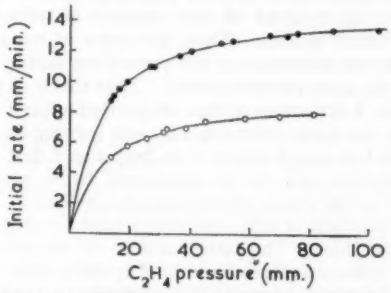

FIG. 2. Variation of initial rate with ethylene pressure. ○ p_{CF_3I} constant at 130 mm. ● p_{CF_3I} constant at 187 mm.

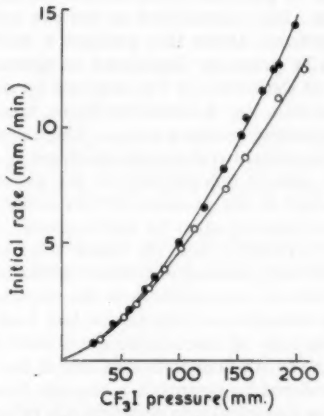

FIG. 3. Variation of initial rate with trifluoroiodomethane pressure. ○ $p_{C_2H_4}$ constant at 31·5 mm. ● $p_{C_2H_4}$ constant at 55·5 mm.

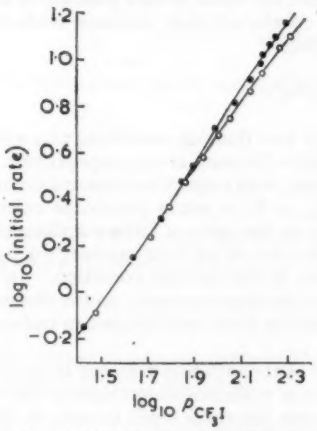

FIG. 4. Variation of log (initial rate) with log (trifluoroiodomethane pressure). ○ $p_{C_2H_4}$ constant at 31·5 mm. ● $p_{C_2H_4}$ constant at 55·5 mm.

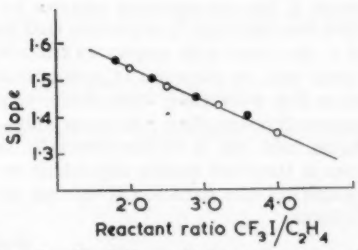

FIG. 5. Variation of slope of curves in Fig. 4 with reactant ratio.

Rate Equation.—The influence of the reactant concentrations on the rate of the reaction was investigated at one temperature, 309°. Here the initial rates of reaction were determined for a series of runs in which the pressure of one reactant was varied with respect to a fixed pressure of the other. In Fig. 2 is shown the variation of rate with pressure of ethylene, with respect to two different fixed pressures of trifluoroiodomethane. Fig. 3 shows the results where the pressure of ethylene is fixed and that of trifluoroiodomethane is varied. From Fig. 2 it is apparent that the rate of addition is markedly dependent on the pressure of ethylene when this is low, while at higher pressures the rate is almost independent of the pressure of ethylene. On the other hand, the rate of reaction is very dependent on the pressure of trifluoroiodomethane throughout the whole of the range investigated (Fig. 3).

From the results shown in Figs. 2 and 3, the empirical rate equation can be written in the form

$$\text{Rate} = k[CF_3I]^x[C_2H_4]^y$$

The question arises as to whether x and y are primarily pressure dependent, or are primarily dependent on the ratio, CF_3I/C_2H_4. If the former is the case the slope of the plot of log (trifluoroiodomethane pressure) against log (rate of reaction) should be equal to the order of reaction with respect to trifluoroiodomethane. Thus, for different fixed pressures of ethylene a series of parallel curves should result. Fig. 4 shows the data from Fig. 3 plotted in this manner; here coincidence of the two curves occurs up to about 68 mm. pressure of trifluoroiodomethane, above this pressure a marked divergence is seen. Thus, the order of reaction cannot be primarily dependent on pressure. If the reactant ratio is the controlling factor the slopes of the curves in Fig. 4 should be similar for the same pressure ratios. That this is so can be seen from Fig. 5 where the slopes, taken from Fig. 4 at various points, are plotted against the corresponding reactant ratio. The coincidence of the lower points in Fig. 4 is inevitable, for here the ratio of trifluoroiodomethane to ethylene is low, and it can be seen from Fig. 2 that the rate is almost independent of the pressure of ethylene and can be considered to be wholly dependent on the pressure of trifluoroiodomethane, at the ratios where coincidence occurs.

Two limiting cases for reaction exist, (1) where the ratio of trifluoroiodomethane to ethylene tends to infinity, and (2) where this ratio tends to zero. The latter case is of theoretical interest only because of telomer formation at low trifluoroiodomethane to ethylene ratios. It is of interest to consider how the empirical rate equation behaves as the reactant ratio varies, and an indication of this can be had from the experimental results. From Fig. 2 it is apparent that the rate of reaction becomes more dependent on the ethylene as the ratio trifluoroiodomethane to ethylene increases, and if the extrapolation of the curve to zero pressure of ethylene is considered to approach a straight-line relationship as the ethylene pressure tends to zero, then the empirical rate equation can be written in the form

$$\text{Rate} = k[CF_3I]^x[C_2H_4]^1.$$

This equation can be considered to operate under the first limiting condition, *i.e.*, where the trifluoroiodomethane to ethylene ratio tends to infinity. Because of the approximate nature of the extrapolation in Fig. 2, a determination of the order, with respect to trifluoroiodomethane, which can be had by equating the two slopes at $p_{C_2H_4} = 0$, is not a justifiable calculation. However, if the rate equation assumes the above form as the ratio of trifluoroiodomethane to ethylene becomes high it is obvious that the slope of the plot of log (rate) against log p_{CF_3I} will equal x, the order with respect to trifluoroiodomethane at the limiting condition. In Fig. 5, it is seen that, as the ratio of trifluoroiodomethane to ethylene increases, so the slopes of the curves in Fig. 4 decrease; thus, it can be presumed that the order with respect to trifluoroiodomethane will be less than 1·35 at very high ratios.

Again from Fig. 2, as the ratio falls, independence of the ethylene pressure is approached; the rate is therefore mainly dependent on the pressure of trifluoroiodomethane in this region. The empirical rate equation governing the reaction when the ratio tends to zero is therefore of the form

$$\text{Rate} = k[CF_3I]^z$$

From Fig. 5 it is seen that the slope of the plot of log (rate) against log p_{CF_3I} increases as the ratio of trifluoroiodomethane to ethylene falls, and for the second limiting case cited above, x will be greater than 1·55.

Thus the rate of reaction is governed by two limiting rate equations, each singly operative where the ratio of trifluoroiodomethane to ethylene approaches the limiting conditions of zero and infinity.

Discussion

The form of the rate equation is complex and on this basis the direct bimolecular reaction,

$$CF_3I + C_2H_4 \longrightarrow CF_3{\cdot}CH_2{\cdot}CH_2I,$$

is discounted. Thus a radical chain mechanism appears most likely, the mode of initiation of the chain being through the thermal decomposition of trifluoroiodomethane. Besides activation through like collisions, activation through collisions of trifluoroiodomethane with ethylene must be postulated, for it is well known that foreign molecules can be quite efficient in promoting thermal decompositions.[4]

$$CF_3I + CF_3I \longrightarrow CF_3I^* + CF_3I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$CF_3I + CF_3I^* \longrightarrow CF_3I + CF_3I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$CF_3I + C_2H_4 \longrightarrow CF_3I^* + C_2H_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$CF_3I^* + C_2H_4 \longrightarrow CF_3I + C_2H_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$CF_3I^* \longrightarrow {\cdot}CF_3 + I{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Steps (3) and (4) appear of little importance when the dependence of rate on the ethylene pressure is considered. Fig. 2 shows that there is very little dependence of the rate on the ethylene pressure when the pressure is appreciable; thus for the sake of simplicity steps (3) and (4) are considered small enough to be neglected.

Propagation *via* steps (6) and (7) is suggested, while telomer formation can be considered to arise through step (8). Since this discussion is concerned with the formation of the 1 : 1-adducts, step (8) can be discounted.

$$CF_3{\cdot} + C_2H_4 \longrightarrow CF_3{\cdot}CH_2{\cdot}CH_2{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$CF_3{\cdot}CH_2{\cdot}CH_2{\cdot} + CF_3I \longrightarrow CF_3{\cdot}CH_2{\cdot}CH_2I + {\cdot}CF_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$CF_3{\cdot}CH_2{\cdot}CH_2{\cdot} + C_2H_4 \longrightarrow CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

Three termination steps are obviously possible: (9), (10), and (11).

$$2{\cdot}CF_3 \longrightarrow C_2F_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$2CF_3{\cdot}CH_2{\cdot}CH_2{\cdot} \longrightarrow [CF_3{\cdot}CH_2{\cdot}CH_2]_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$CF_3{\cdot} + CF_3{\cdot}CH_2{\cdot}CH_2{\cdot} \longrightarrow CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}CF_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

Steps 1, 2, 5, 6, 7, 9, 10, and 11 being assumed the important steps controlling the reaction scheme, the following theoretical rate equation is derived.

$$-dp/dt = d[CF_3{\cdot}CH_2{\cdot}CH_2I]/dt = k_7[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}][CF_3I] \quad . \quad . \quad (12)$$

Long chains being assumed, there will be a balance between the propagating steps (6) and (7), at the stationary-state condition.

Thus, $$k_7[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}][CF_3I] = k_6[{\cdot}CF_3][C_2H_4] \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

Also the rate of formation of radicals will be equal to their rate of disappearance.

Thus, $$k_5[CF_3I^*] = k_9[{\cdot}CF_3]^2 + 2k_{11}[{\cdot}CF_3][CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}] + k_{10}[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}]^2 \quad (14)$$

The plausible assumption being made that $k_9k_{10} \simeq k_{11}^2$, this can be substituted into eqn. (14) and the root taken.

Thus, $$(k_5[CF_3I^*])^{\frac{1}{2}} = k_9^{\frac{1}{2}}[{\cdot}CF_3] + k_{10}^{\frac{1}{2}}[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}] \quad . \quad . \quad . \quad . \quad . \quad (15)$$

From eqn. (13) we have

$$[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}] = k_6[{\cdot}CF_3][C_2H_4]/k_7[CF_3I] \quad . \quad . \quad . \quad . \quad . \quad (16)$$

[4] Bell, Robinson, and Trenwith, *J.*, 1957, 1474; Lindar and Hinshelwood, *Proc. Roy. Soc.*, 1955, *A*, **231**, 162; Volpe and Johnston, *J. Amer. Chem. Soc.*, 1956, **78**, 3903.

By substitution of $[CF_3{\cdot}CH_2{\cdot}CH_2{\cdot}]$ from eqn. (16) into eqn. (15) we have,

$$(k_5[CF_3I^*])^{\frac{1}{2}} = k_9^{\frac{1}{2}}[{\cdot}CF_3] + k_{10}^{\frac{1}{2}}k_6[{\cdot}CF_3][C_2H_4]/k_7[CF_3I] \quad . \quad . \quad . \quad . \quad (17)$$

Now, $d[CF_3I^*]/dt = 0 = k_1[CF_3I]^2 - k_2[CF_3I][CF_3I^*] - k_5[CF_3I^*]$ . . . . . (18)

Thus,
$$(k_5[CF_3I^*])^{\frac{1}{2}} = [CF_3I]\left(\frac{k_5k_1}{k_5 + k_2[CF_3I]}\right)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad (19)$$

Combination of equations (17) and (19) gives

$$[CF_3I]\left(\frac{k_5k_1}{k_5 + k_2[CF_3I]}\right)^{\frac{1}{2}} = [{\cdot}CF_3]\left(k_9^{\frac{1}{2}} + \frac{k_{10}^{\frac{1}{2}}k_6[C_2H_4]}{k_7[CF_3I]}\right) \quad . \quad . \quad . \quad (20$$

Hence,
$$[{\cdot}CF_3] = \frac{k_7[CF_3I]^2}{k_9^{\frac{1}{2}}k_7[CF_3I] + k_{10}^{\frac{1}{2}}k_6[C_2H_4]}\left(\frac{k_1k_5}{k_5 + k_2[CF_3I]}\right)^{\frac{1}{2}} \quad . \quad . \quad (21)$$

Now, from eqns. (12) and (13), the rate of reaction may be written:

$$-dp/dt = k_6[{\cdot}CF_3][C_2H_4] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (22)$$

and substituting for $[{\cdot}CF_3]$ from eqn. (21) we obtain

$$\text{Rate} = -\frac{dp}{dt} = \frac{k_6k_7[CF_3I]^2[C_2H_4]}{k_9^{\frac{1}{2}}k_7[CF_3I] + k_{10}^{\frac{1}{2}}k_6[C_2H_4]}\left(\frac{k_1k_5}{k_5 + k_2[CF_3I]}\right)^{\frac{1}{2}} \quad . \quad . \quad (23)$$

It is obvious that eqn. (23) may be written in two limiting forms, *i.e.* where the ratio $[CF_3I]/[C_2H_4]$ is high or low.

Case 1. *Ratio* $[CF_3I]/[C_2H_4]$ *high.*—Obviously $k_9^{\frac{1}{2}}k_7[CF_3I] \gg k_{10}^{\frac{1}{2}}k_6[C_2H_4]$ and as the reactant ratio tends to infinity, so the rate equation can be written as

$$-\frac{dp}{dt} = \left(\frac{k_6[CF_3I][C_2H_4]}{k_9^{\frac{1}{2}}}\right)\left(\frac{k_1k_5}{k_5 + k_2[CF_3I]}\right)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad (24)$$

Experimentally it has been shown that as the limiting condition is approached the empirical rate equation is of the form,

$$\text{Rate} = k[CF_3I]^x[C_2H_4]^1 \text{ where } x < 1{\cdot}35,$$

this is in excellent agreement with the limiting theoretical eqn. (24).

Case 2. *Ratio* $[CF_3I]/[C_2H_4]$ *low.*—Obviously $k_9^{\frac{1}{2}}k_7[CF_3I] \ll k_{10}^{\frac{1}{2}}k_6[C_2H_4]$ and as the reactant ratio tends to its limiting value so the rate eqn. (23) tends to

$$-\frac{dp}{dt} = \left(\frac{k_7[CF_3I]^2}{k_{10}^{\frac{1}{2}}}\right)\left(\frac{k_1k_5}{k_5 + k_2[CF_3I]}\right)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad (25)$$

Experimentally it has been shown that as the conditions for case 2 are approached the empirical rate equation is of the form

$$\text{Rate} = k[CF_3I]^x, \text{ where } x > 1{\cdot}55.$$

Again this is in agreement with the theoretical eqn. (25). The general equation for the

rate of reaction, eqn. (23), can be rearranged in the forms (26) and (27), where κ, κ', and κ'' are combinations of velocity constants.

$$\frac{\text{Rate}}{\kappa} = \frac{[C_2H_4][CF_3I]^2}{([C_2H_4] + \kappa'[CF_2I])(1 + \kappa''[CF_2I])^{\frac{1}{2}}} \quad . \quad . \quad . \quad . \quad . \quad (26)$$

$$\frac{\kappa}{\text{Rate}} = \frac{(1 + \kappa''[CF_3I])^{\frac{1}{2}}}{[CF_3I]^2} + \frac{\kappa'(1 + \kappa''[CF_3I])^{\frac{1}{2}}}{[CF_3I]} \cdot \frac{1}{[C_2H_4]} \quad . \quad . \quad . \quad (27)$$

A plot of the results shown in Fig. 2, in the form 1/rate against $1/[C_2H_4]$, which corresponds to eqn. (27), is given in Fig. 6. The straight-line relationship as predicted by eqn. (27) is further evidence for the validity of the reaction mechanism suggested.

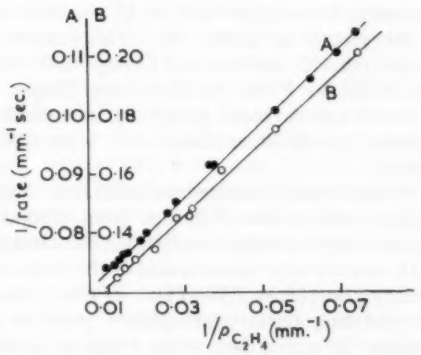

FIG. 6. Variation of 1/rate with $1/p_{C_2H_4}$ ○ p_{CF_3I} constant at 130 mm. ● p_{CF_3I} constant at 187 mm.

A series of experiments designed to measure accurately the initial slopes of the curves in Fig. 2 where the pressure of ethylene tends to zero would yield values corresponding to

$$\frac{k_6(k_5k_1)^{\frac{1}{2}}[CF_3I]}{k_9^{\frac{1}{2}}(k_5 + k_2[CF_3I])^{\frac{1}{2}}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (28)$$

By using different olefins a value corresponding to eqn. (28) could be obtained for each olefin. In these values the only uncommon velocity constant would be k_6, hence this method could be used to determine the differences in activation energy for the addition of trifluoromethyl radicals to various π bond systems.

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980. *The Reactions of Di- and Tri-tertiary Phosphines with the Hexacarbonyls of Metals of Group VI.*

By J. Chatt and H. R. Watson.

Ditertiary phosphines react with the hexacarbonyls of chromium, molybdenum, and tungsten, replacing either two or four carbon monoxide molecules. Tritertiary phosphines replace three. Complete expulsion of carbonyl groups was not achieved. *cis-trans*-Isomerism is exhibited by the substituted chromium derivatives, but not by those of molybdenum or tungsten. The carbonyl absorption frequencies in the 1700—2100 cm.$^{-1}$ range, and dipole moments, are recorded.

In view of the relative ease with which tertiary diphosphines replace all of the carbon monoxide from nickel carbonyl,[1] we have examined their reactions with the carbonyls of the metals of Group VI. The reactions of monodentate tertiary phosphines and phosphites with carbonyls of Group VI metals are referred to in papers by Abel, Bennett, and Wilkinson [2] and by Matthews, Magee, and Wotiz.[3] They show that replacement of one or two carbonyl groups by monodentate ligands proceeds readily, whereas a third carbonyl group is expelled only with difficulty. Further replacement has not been effected.

Using *o*-phenylenebisdimethylarsine, Nigam, Nyholm, and Stiddard [4] were able to displace four carbonyl groups from chromium, molybdenum, and tungsten carbonyls. We now report similar results with the ditertiary phosphines (I), (II; R = Et or Ph), and (III), and also our examination of the replacement of carbon monoxide by the tridentate tertiary phosphines (IV—VI). In every case simple replacement of carbon monoxide by the chelating tertiary phosphines [with *m* phosphorus(III) atoms] occurred as follows, yielding the mixed derivatives listed in Table 1.

$$n\ \text{Polyphosphine} + \text{M(CO)}_6 \longrightarrow [\text{M(Polyphosphine)}_n(\text{CO})_{6-nm}] + nm\text{CO}$$

$CH_2(PPh_2)_2$	$(CH_2{\cdot}PR_2)_2$	$o\text{-}C_6H_4(PEt_2)_2$
(I)	(II)	(III)
$Ph{\cdot}P(o\text{-}C_6H_4{\cdot}PEt_2)_2$	$Ph{\cdot}P(C_2H_4{\cdot}PPh_2)_2$	$Me{\cdot}C(CH_2{\cdot}PPh_2)_3$
(IV)	(V)	(VI)

Ease of Replacement of Carbonyl Groups.—Previous work suggests that expulsion of carbonyl groups by tervalent phosphorus compounds proceeds stepwise with increasing difficulty, until there remain three carbonyl groups which cannot be removed by monodentate ligands. Electronegative substituents on the phosphorus atom favour this replacement.

Ditertiary phosphines react similarly. Replacement of two carbonyl groups occurs readily, and with the diphosphine (II; R = Et) no further replacement occurs. The more electronegative diphosphines (II; R = Ph) and (III) replace a third carbonyl, and even a fourth carbonyl group; the remaining two carbonyl groups are very strongly bound and have resisted all our attempts to replace them. With the tetracarbonyl derivatives of chromium replacement is difficult to effect and, under the experimental conditions used for the molybdenum and tungsten analogues, only minute yields of dicarbonyl derivatives were obtained. Therefore they were prepared by using the relatively ready displacement of mesitylene from mesitylenechromium tricarbonyl. When the arenemetal tricarbonyl was heated at atmospheric pressure with two equivalents of the diphosphines (I), (II; R = Ph), or (III) it gave the dicarbonyls in fair yield, with considerable proportions of

[1] Chatt and Hart, *J.*, 1960, 1378.
[2] Abel, Bennett, and Wilkinson, *J.*, 1959, 2323.
[3] Matthews, Magee, and Wotiz, *J. Amer. Chem. Soc.*, 1959, **81**, 2273.
[4] Nigam, Nyholm, and Stiddard, *J.*, 1960, 1803.

tetracarbonyl derivatives. This was unexpected because nitrogen was passed rapidly through the reaction mixture to strip away mesitylene and would also have removed any free carbon monoxide. Apparently these carbonyl compounds can take part in reactions in which a carbonyl group of one molecule undergoes exchange with a ligand of another molecule.

The tritertiary phosphines (IV—VI) readily expel three molecules of carbon monoxide, to give the triphosphinemetal tricarbonyls, but further replacement does not occur in the presence of an excess of the phosphine, even at 250°. The strong bonding of the remaining three carbonyl groups is shown further by the reaction of the tritertiary phosphine (VI) with the tetracarbonyl (XVII) (Table 1) to give the tricarbonyl (XXXIII). The triphosphine presumably replaces one carbonyl group and then it expels the chelated ditertiary phosphine, in preference to the remaining carbonyls. No reaction occurs between the triphosphine (VI) and the dicarbonyl (XXVII).

We believe that total replacement in carbonyls of Group VI metals by di- or tri-tertiary phosphines is not possible. Nevertheless, products of the formula $[M(diphosphine)_3]$ (M = Cr, Mo, and W) have been obtained by other methods [5] and are thermally stable.

General Properties of the Derivatives.—All crystallise well from solution. The tetracarbonyls are more soluble in non-polar than in polar solvents, being very soluble in chloroform or benzene, and sparingly so in ethanol or methanol. Solubility decreases with rising molecular weight of the component tertiary phosphine but does not appear to vary much between the corresponding derivatives of the three metals. The dicarbonyls and tricarbonyls have solubility characteristics similar to those of the tetracarbonyls, but in general are much less soluble. The compounds are non-conductors in nitrobenzene solution.

In the absence of light, the compounds are not obviously oxidised by air, even in solution, and in this respect differ from the corresponding ditertiary arsine derivatives.[4] In light and air, the solids darken slowly, and in solution they slowly deposit oxidised material. The derivative (XXIX) is oxidised faster than the others and had to be recrystallised in a nitrogen atmosphere. Light, in the absence of oxygen, appears to have no effect on the compounds: under nitrogen their solutions are unchanged when illuminated by a strong ultraviolet source for long periods.

The compounds are oxidised when heated in air, and therefore melting points were determined in evacuated tubes. In the absence of air they are thermally stable and most of them, even those of high m. p., appear to melt without decomposition. In attempts to achieve complete replacement we have heated dicarbonyls such as (XXVII) with the component ditertiary phosphine *in vacuo* for two weeks at 200°, or at this temperature for some days in a quartz vessel with strong ultraviolet illumination; the reactants were unchanged.

Configurations of Derivatives.—Dipole moments and infrared spectra have been used to elucidate the configurations of the tetra-, tri-, and di-carbonyl complexes.

All of the derivatives of molybdenum and tungsten have configurations with the greatest possible number of carbonyl groups in relative *cis*-positions. In the tetracarbonyl series, the chelate ligands impose such a configuration, but the molybdenum and tungsten derivatives (XX and XXI) of the monodentate phosphine ($PPhEt_2$) also have *cis*-phosphorus configurations. Their dipole moments in benzene are constant, indicating no spontaneous isomerisation, and the values are close to those of the corresponding derivatives of the chelating diphosphine (III).

The dicarbonyl complexes of molybdenum and tungsten have dipole moments in the region 6·15—6·7 D, in accordance with the *cis*-dicarbonyl structure. No evidence of a *trans*-configuration has been observed.

In order to satisfy the steric requirements of the triphosphine (VI) the three carbonyl

[5] Chatt and Watson, *Proc. Chem. Soc.*, 1960, 243, and unpublished work.

groups in the derivatives (XXXII), (XXXIII), and (XXXIV) must occupy positions mutually at right angles. The observed dipole moment, 8·75 D, of the tricarbonyl (XXXIII) supports this conclusion. The infrared spectra of the derivatives (XXX) and (XXXI) indicate that these also have the carbonyl groups in *cis*-positions although the constituent triphosphines (IV) and (V) are able to span either edge or face positions.

In contrast to the molybdenum and tungsten derivatives, all of the chromium compounds in which *cis-trans*-isomerism is possible have shown evidence of such isomerism, by spontaneous change of dipole moment or of infrared spectrum in solution.

Where two values of the dipole moment are quoted in Table 1, they represent, respectively, the moment obtained by extrapolation to zero time of dissolution of the sample, and the apparent moment when equilibrium has been reached. Measurements at timed intervals show that intermediate values lie on an exponential curve. The isomerisation is shown clearly by the dicarbonyl derivatives (XXV) and XXVI). The moment of the pure *cis*-isomer, 6·2 D, decreases to a value of 4·85 D, whereas that of the *trans*-isomer,

TABLE 1.

Some physical properties of new phosphorus-substituted group VI carbonyls.

Compound		M. p.	Colour	Dipole moment (D)
$[Cr(CO)_4C_6H_4(PEt_2)_2]$	VII	116—116·5°	White	—
$[Mo(CO_4C_6H_4(PEt_2)_2]$	VIII	106·5—107	,,	—
$[W(CO)_4C_6H_4(PEt_2)_2]$	IX	121·5—122	Pale yellow	—
$[Cr(CO)_4o\text{-}C_6H_4(PEt_2)_2]$	X	162—164·5	White	7·6
$[Mo(CO)_4o\text{-}C_6H_4(PEt_2)_2]$	XI	181·5—182	,,	7·8
$[W(CO)_4o\text{-}C_6H_4(PEt_2)_2]$	XII	190·5—191	,,	8·25
$[Cr(CO)_4CH_2(PPh_2)_2]$	XIII	170·5—171·5	Yellow	—
$[Mo(CO)_4CH_2(PPh_2)_2]$	XIV	195·5—196	Pale yellow	—
$[W(CO)_4CH_2(PPh_2)_2]$	XV	200·5—201·5	,,	—
$[Cr(CO)_4C_2H_4(PPh_2)_2]$	XVI	211—212	,,	—
$[Mo(CO)_4C_2H_4(PPh_2)_2]$	XVII	193—194	White	—
$[W(CO)_4C_2H_4(PPh_2)_2]$	XVIII	208—209	Pale yellow	—
cis-$[Cr(CO)_4(PPhEt_2)_2]$	XIX	95—95·5	Lemon-yellow	~5·0 ⟶ 3·3
cis-$[Mo(CO)_4(PPhEt_2)_2]$	XX	98·5—99	Pale buff	6·95
cis-$[W(CO)_4(PPhEt_2)_2]$	XXI	104	Pale yellow	7·25
cis-$[Cr(CO)_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ ...	XXII	263·5—266·5	Orange	—
cis-$[Mo(CO)_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ ...	XXIII	257—258	Bright yellow	6·4
cis-$[W(CO)_2\{o\text{-}C_6H_4(PEt_2)_2\}_2]$ ...	XXIV	270—272	,,	6·6
cis-$[Cr(CO)_2\{C_2H_4(PPh_2)_2\}_2]$	XXV	280—280·5	Pale orange	6·2 ⟶ 4·85
trans-$[Cr(CO)_2\{C_2H_4(PPh_2)_2\}_2]$ ...	XXVI	279—280	Vermilion red	0·95 ⟶ 4·1
cis-$[Mo(CO)_2\{C_2H_4(PPh_2)_2\}_2]$	XXVII	324—325	Yellow	6·15
cis-$[W(CO)_2\{C_2H_4(PPh_2)_2\}_2]$	XXVIII	320—323	Bright yellow	6·7
cis-$[Cr(CO)_2\{CH_2(PPh_2)_2\}_2]$	XXIX	289	Orange	6·55 ⟶ 5·4
$[Mo(CO)_3Ph\cdot P(o\text{-}C_6H_4\cdot PEt_2)_2]$ ...	XXX	268·5—269	Pale yellow	—
$[Mo(CO)_3Ph\cdot P(C_2H_4\cdot PPh_2)_2]$ ...	XXXI	261·5—263	White	—
$[Cr(CO)_3Me\cdot C(CH_2\cdot PPh_2)_3]$	XXXII	362 *	Pale yellow	—
$[Mo(CO)_3Me\cdot C(CH_2\cdot PPh_2)_3]$	XXXIII	378—380 *	White	8·75
$[W(CO)_3Me\cdot C(CH_2\cdot PPh_2)_3]$	XXXIV	>400 *	,,	—

* After decomposition.

initially 0·95 D, increases to 4·1 D, indicating that the equilibrium mixture contains about equal amounts of both isomers.

The intensely vermilion-red *trans*-compound (XXVI) is the only isolated *trans*-dicarbonyl of a Group VI metal. It is isomerised by adding an excess of methanol to its red solution in benzene or chloroform. The solution becomes yellow immediately and the *cis*-isomer separates completely. This change is accompanied by some side reaction, since no *trans*-isomer remains and the yield of *cis*-isomer is variable. On the other hand, complete reconversion of the *cis*- into the *trans*-isomer is attained by heating its yellow solution in benzene, toluene, or chloroform, whereupon it rapidly becomes deep red; the *trans*-isomer may then be recovered by evaporation. When the solid *cis*-compound is heated *in vacuo* it gradually becomes red and melts finally at the m. p. of the *trans*-compound. The change from *trans* to *cis* is very rapid at room temperature in 1,2-dichloroethane.

Rapid dissolution of a sample of the *trans*-compound in this solvent, followed by immediate inspection of the carbonyl infrared stretching frequencies, has shown that although the intensities of the carbonyl absorption bands of the *cis*-isomer increase slightly during measurement, no band attributable to a *trans*-isomer is detectable. Both the potassium bromide disc and the Nujol mull prepared from the *trans*-compound are yellow, and both transmit the spectrum of the *cis*-compound.

The *cis*-derivative (XXIX) of the methylene diphosphine (I) undergoes similar changes. However, the colour changes are reversible, and attempts to isolate the *trans*-isomer failed. The *cis–trans* change of the dicarbonyl (XXII) has been inferred from its infrared absorption characteristics (see below).

The few dicarbonyl derivatives of Group VI metals which have been reported previously appear to have only *cis*-carbonyl configurations.[6,7] Even dicarbonylbis-(*o*-phenylenebis-dimethylarsine)chromium, similar in constitution to the dicarbonyl derivatives of our series, appears only in the *cis*-form.[4]

The apparent dipole moment of the *cis*-chromium tetracarbonyl (XIX) in benzene solution decreases with time, finally attaining a steady value, but no *trans*-isomer has been

TABLE 2.

Carbonyl infrared absorption frequencies (cm.$^{-1}$) in 1,2-dichloroethane.

Formula	M = Mo	M = W	M = Cr
$[M(CO)_4C_2H_4(PPh_2)_2]$	2020s	2016s	2009s
	1919sh	1912sh	1914sh
	1907vs	1901vs	1899vs
	1881s	1876s	1877s
$[M(CO)_4CH_2(PPh_2)_2]$	2020s	2013s	2006s
	1920sh	1909sh	1915s
	1907vs	1902vs	1897vs
	1879s	1871s	1875s
$[M(CO)_4o\text{-}C_6H_4(PEt_2)_2]$	2014s	2011s	2001s
	1912sh	1905sh	1906sh
	1896vs	1887vs	1884vs
	(—)sh	(—)sh	(—)sh
$[M(CO)_4(PPhEt_2)_2]$	2012s	2008s	1999
	1907sh	1900sh	1897sh
	1895vs	1885vs	1873vs
	1866s	1862s	(—)sh
$[M(CO)_4C_2H_4(PEt_2)_2]$	2012s	2008s	2000s
	1909sh	1901sh	1905s
	1891vs	1882vs	1880vs
	(1873)sh	(1866)sh	(—)sh
$[M(CO)_3\{C_2H_4(PPh_2)_2\}_2]$	1852s	1847s	1848s
	1786s	1782s	1708s
$[M(CO)_3\{o\text{-}C_6H_4(PEt_2)_2\}_2]$	1843s	1832s	1826s
	1774s	1766s	1760s
$[M(CO)_3Me{\cdot}C(CH_2{\cdot}PPh_2)_3]$	1930s	1930s	1905s
	1834s	1834s	1830s
$[Mo(CO)_3Ph{\cdot}P(C_2H_4{\cdot}PPh_2)_2]$	1937s		
	1848s		
$[Mo(CO)_3Ph{\cdot}P(o\text{-}C_6H_4{\cdot}PEt_2)_2]$	1937s		
	1844s		

isolated. Different samples of this compound, of the same m. p., give different values of dipole moment (the highest obtained are recorded in Table 1) and it is probable that these samples contained different proportions of *trans*-isomer as impurity. The *cis*-molybdenum and tungsten analogues (XX) and (XXI), show no signs of isomerisation, but a few examples of isomerisation of this type of derivative have appeared recently. The *cis*-forms of the Group VI tetracarbonyls, $M(CO)_4L_2$, are usually isolated, but Poilblanc and Bigorgne [8] were able to isolate pure *cis*- and *trans*-forms of $Mo(CO)_4(PEt_3)_2$ and obtained

[6] Weiss and Hübel, *J. Inorg. Nuclear Chem.*, 1959, **11**, 42.
[7] Fischer, Palm, and Fritz, *Chem. Ber.*, 1959, **92**, 2645.
[8] Poilblanc and Bigorgne, *Compt. rend.*, 1960, **250**, 1064.

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evidence of isomeric change of $Mo(CO)_4(PPh_3)_2$ and $W(CO)_4(PEt_3)_2$. These compounds isomerise in solution. Hieber and Peterhans [9] have also shown that the bistriphenylphosphine tetracarbonyls of chromium, molybdenum, and tungsten exist in the *trans*-form.

Infrared Absorption Spectra (with D. M. Adams).—The infrared absorption spectra of the substituted carbonyls in 1,2-dichloroethane solution have been measured in the 1700—2100 cm.$^{-1}$ region (Table 2). The main features of the infrared spectra of metal carbonyls and their derivatives have already been determined but this work presents the first detailed series of Group VI carbonyls, containing the same ligand atom as substituent.

Table 2 is laid out so that the carbonyl frequencies (ν_{C-O}) decrease downwards and to the right in each half of the Table. In corresponding compounds of these series of di- and tetra-carbonyls the carbonyl frequencies decrease in the order Mo > W > Cr. This does not parallel that (Cr > Mo > W) shown by the related tricarbonyl derivatives studied by Wilkinson and his colleagues,[2] or that of the hexacarbonyls in 1,2-dichloroethane (Mo > Cr > W). The differences between the corresponding frequencies in the compounds of these three metals are small, and these differences in sequence probably have little significance.

Electronegative groups attached to the phosphorus atoms cause progressive decrease in ν_{C-O}, presumably by withdrawing electrons from the metal and so increasing the contribution of the triply bonded resonance form, M–C≡O, relative to the doubly-bonded form M=C=O. This effect is a general effect.[1,2,10]

Tetracarbonyl Complexes.—The symmetry of these complexes is C_{2v}, the four carbonyl stretching vibrations being distributed amongst the symmetry classes of the point group as follows: [7] $\tau = 2A_1 + B_1 + B_2$. All are infrared active.

These vibrations may be considered as two pairs, originating from (i) symmetric (A_1) and antisymmetric (B_1) modes of the two *trans*-carbonyl groups, and (ii) symmetric (A_1) and antisymmetric (B_2) modes of the two *cis*-carbonyl groups. There will however be some interaction between these modes and this will be greatest in the case of the two A_1 modes. The antisymmetric modes are expected to lie at higher frequencies than their corresponding A_1 modes, which will probably be quite close together. It is found in practice that one sharp band is present near 2000 cm.$^{-1}$ and a broad band showing indications of three contributions centred near 1850 cm.$^{-1}$. The 2000 cm.$^{-1}$ band must be due to either the B_1 or the B_2 mode, the other antisymmetric mode being part of the broad band, in which the A_1 components will probably have been mutually shifted by Fermi resonance.

Since interaction of the B_1 and the B_2 mode with each other or with A_1 modes will be slight, the single band near 2000 cm.$^{-1}$ indicates that one of the pairs of carbonyl groups has a higher force constant than the other. On the basis that carbonyl groups have a large *trans*-effect it seems likely that this is the *trans*-pair.

Dicarbonyl Derivatives.—In the *cis*-dicarbonyl derivatives two strong carbonyl frequencies are observed. These are lowered very considerably with respect to the parent carbonyl and are within the range usually attributed to bridging carbonyls (the same effect has been noted [2] with tricarbonyl derivatives of Group VI). It is apparent that the two remaining carbonyl groups are able to share a much greater proportion of the available metal *d*-electrons; the resulting strong bonding to the metal explains their great resistance to substitution.

The chromium dicarbonyl (XXII) gives a spectrum containing three carbonyl absorption bands. Two, at 1826 and 1760 cm.$^{-1}$, decrease in intensity with time, and the third, at 1844 cm.$^{-1}$, increases in intensity. The highest value is probably the single absorption band of the (unisolated) *trans*-dicarbonyl, and it increases in intensity during a change in solution from pure *cis*- to an equilibrium mixture of *cis*- and *trans*-forms.

Tricarbonyl Derivatives.—Absorption frequencies of tricarbonyl derivatives of Group

[9] Hieber and Peterhans, *Z. Naturforsch*, 1959, **14b**, 462.
[10] Meriwether and Fiene, *J. Amer. Chem. Soc.*, 1959, **81**, 4200.

Vol. 1961, page 4984, line 23. *For* τ *read* Γ; *also delete two following paragraphs from:* These vibrations may . . . *to* . . . is the *trans* pair.

VI metals have been discussed previously.[2] The compounds of the present series are of unequivocal structure and the results obtained from them are in accord with previous work.

Experimental

M. p.s are corrected and were determined in evacuated tubes. Molecular weights were determined ebullioscopically and in acetone unless otherwise stated. Microanalyses were carried out in these laboratories; normal combustion frequently gave low carbon values, probably caused by partial formation of stable metal carbides; admixture of the sample with potassium dichromate overcame this difficulty. The diphosphines $(CH_2{\cdot}PR_2)_2$ (R = Et or Ph) were prepared as described by Chatt and Hart,[11] *o*-$C_6H_4(PEt_2)_2$ and $Ph{\cdot}P(o\text{-}C_6H_4PEt_2)_2$ as described by Hart,[12] and $CH_2(PPh_2)_2$ by a modification of Issleib and Muller's method.[13] The preparation of $Me{\cdot}C(CH_2{\cdot}PPh_2)_3$ and $Ph{\cdot}P(C_2H_4{\cdot}PPh_2)_2$ will be detailed later.[14] A representative selection of the carbonyl compounds was shown to be electrically non-conducting in nitrobenzene.

Tetracarbonyl Derivatives.—These were prepared by heating a slight excess of the metal hexacarbonyl with the tertiary phosphine in a sealed evacuated tube of such dimensions that at the temperature used the final pressure of evolved carbon monoxide did not exceed 10 atm.

Tetracarbonyl-1,2-bisdiethylphosphinoethanechromium (VII). A mixture of chromium carbonyl and the phosphine was heated at 150—160° for 4·5 hr., and the cooled crystalline mass was recrystallised from ethanol to yield the *tetracarbonyl* (85%) (Found: C, 45·2; H, 6·7%; *M*, 355. $C_{14}H_{24}CrO_4P_2$ requires C, 45·4; H, 6·5%; *M*, 370). The compound distils unchanged at 140° (bath)/0·02 mm. The following compounds were similarly prepared; the heating periods are in parentheses.

Tetracarbonyl-1,2-bisdiethylphosphinoethanemolybdenum (VIII) (6 hr.) The cooled brown crystalline mass recrystallised from light petroleum (b. p. 80—100°), to give a yellow solid (68%) which on recrystallisation from methanol yielded the pure *tetracarbonyl* (Found: C, 40·4; H, 5·8%; *M*, 360. $C_{14}H_{24}MoO_4P_2$ requires C, 40·6; H, 5·8%; *M*, 414).

Tetracarbonyl-1,2-bisdiethylphosphinoethanetungsten (IX) (12 hr.). The cooled product, when recrystallised from ethanol, gave the *tetracarbonyl* (79%). Further recrystallisation followed by elution in ether through alumina afforded the pure compound (Found: C, 33·3; H, 4·8. $C_{14}H_{24}O_4P_2W$ requires C, 33·5; H, 4·8%).

Tetracarbonyl-o-phenylenebisdiethylphosphinechromium (X) (5 hr.). Crystallisation of the product from ethanol gave the *tetracarbonyl* (62%), purified by repeated recrystallisation from light petroleum (b. p. 80—100°) (Found: C, 51·7; H, 5·9. $C_{18}H_{24}CrO_4P_2$ requires C, 51·7; H, 5·8%).

Tetracarbonyl-o-phenylenebisdiethylphosphinemolybdenum (XI) (3 hr.). An excess of molybdenum carbonyl was sublimed from the product, and recrystallisation from light petroleum (b. p. 80—100°) gave the pure *tetracarbonyl* (70%) (Found: C, 47·1; H, 5·35%; *M*, 450. $C_{18}H_{24}MoO_4P_2$ requires C, 46·8; H, 5·2%; *M*, 462).

Tetracarbonyl-o-phenylenebisdiethylphosphinetungsten (XII) (7 hr.). The product (77%) gave the *tetracarbonyl* which was purified by repeated recrystallisation from methanol (Found: C, 38·7; H, 4·5. $C_{18}H_{24}O_4P_2W$ requires C, 39·3; H, 4·4%).

Tetracarbonylbisdiphenylphosphinomethanechromium (XIII) (12 hr.) The *tetracarbonyl* (77%) was purified by repeated recrystallisation from light petroleum (b. p. 80—100°) (Found: C, 63·6; H, 4·15%; *M* in chloroform, 559. $C_{29}H_{22}CrO_4P_2$ requires C, 63·5; H, 4·0%; *M*, 548·5).

Tetracarbonylbisdiphenylphosphinomethanemolybdenum (XIV) (8 hr.). Recrystallisation from acetone gave the *tetracarbonyl* (97%) which repeatedly recrystallised from light petroleum (b. p. 80—100°) (Found: C, 58·65; H, 4·0%; *M* in chloroform, 600. $C_{29}H_{22}MoO_4P_2$ requires C, 58·8; H, 3·7%; *M*, 592).

Tetracarbonylbisdiphenylphosphinomethanetungsten (XV) (8 hr.). Recrystallisation from acetone gave the *tetracarbonyl* (93%) (Found: C, 50·55; H, 3·3; *M*, 654, 647. $C_{29}H_{22}O_4P_2W$ requires C, 51·2; H, 3·3%; *M*, 680).

Tetracarbonyl-1,2-bisdiphenylphosphinoethanechromium (XVI) (12 hr.). Recrystallisation from acetone gave the *tetracarbonyl* (71%), which was purified by further recrystallisation from

[11] Chatt and Hart, *J.*, 1960, 1378.
[12] Hart, *J.*, 1960, 3324.
[13] Issleib and Muller, *Chem. Ber.*, 1959, **92**, 3175.
[14] Hewertson and Watson, unpublished work.

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acetone (Found: C, 64·3; H, 4·6%; *M*, 539. $C_{30}H_{24}CrO_4P_2$ requires C, 64·1; H, 4·3%; *M*, 562·5).

Tetracarbonyl-1,2-*bisdiphenylphosphinoethanemolybdenum* (XVII). The reactants were kept at 150° for 5 hr., then at 170° for 4 hr. The *tetracarbonyl* (67%) was obtained as prisms from acetone (Found: C, 59·3; H, 4·2. $C_{30}H_{24}MoO_4P_2$ requires C, 59·4; H, 4·0%).

Tetracarbonyl-1,2-*bisdiphenylphosphinoethanetungsten* (XVIII) (17 hr.). Recrystallisation from acetone–methanol gave the *tetracarbonyl* (67%), purified by further recrystallisation (Found: C, 52·1; H, 3·55%; *M*, 675. $C_{30}H_{24}O_4P_2W$ requires C, 51·9; H, 3·5%; *M*, 694).

cis-*Tetracarbonylbis*(*diethylphenylphosphine*)*chromium* (XIX) (8 hr.). Recrystallisation from ethanol–methanol gave the *tetracarbonyl* (XIX) (63%) which was purified by repeated recrystallisation (Found: C, 58·2; H, 6·3%; *M*, 489, 515. $C_{24}H_{30}CrO_4P_2$ requires C, 58·1; H, 6·1%; *M*, 496·5).

cis-*Tetracarbonylbis*(*diethylphenylphosphine*)*molybdenum* (XX) was prepared similarly (81%) and recrystallised from light petroleum (b. p. 60—80°) (Found: C, 53·5; H, 5·9. $C_{24}H_{30}MoO_4P_2$ requires C, 53·3; H, 5·6%).

cis-*Tetracarbonylbis*(*diethylphenylphosphine*)*tungsten* (XXI) was prepared similarly (58%) and repeatedly recrystallised from light petroleum (b. p. 60—80°) (Found: C, 45·6; H, 4·8%; *M*, 610, 606. $C_{24}H_{30}O_4P_2W$ requires C, 45·9; H, 4·8%; *M*, 628).

Dicarbonyl Derivatives.—cis-*Dicarbonyldi*-o-*phenylenebisdiethylphosphinechromium* (XXII). Tricarbonylmesitylenechromium and the ditertiary phosphine (2 equiv.) were mixed and heated in a nitrogen atmosphere at 195° for 5 hr.; recrystallisation of the product from ethanol gave a low yield of the *dicarbonyl* (Found: C, 58·6; H, 7·9. $C_{30}H_{48}CrO_2P_4$ requires C, 58·4; H, 7·85%).

cis-*Dicarbonyldi*-o-*phenylenebisdiethylphosphinemolybdenum* (XXIII). A mixture of the tetracarbonyl (XI) and the ditertiary phosphine (one equiv.), maintained under nitrogen and illuminated by a strong ultraviolet source, was heated at 220° for 16 hr., after which no gas evolution was discernible. Recrystallisation of the cooled mass from ethanol gave the *dicarbonyl* (51%) (Found: C, 54·55; H, 7·3%; *M* in chloroform, 653. $C_{30}H_{48}MoO_2P_4$ requires C, 54·55; H, 7·3%; *M*, 661).

cis-*Dicarbonyldi*-o-*phenylenebisdiethylphosphinetungsten* (XXIV). A mixture of the tetracarbonyl (XII) and the diphosphine (one equiv.) was heated in a sealed evacuated tube at 230° for 60 hr. Recrystallisation of the product from ethanol gave the bright yellow *dicarbonyl* (36%), m. p. 270—272° (becoming orange above 100°) after further recrystallisation (Found: C, 48·5; H, 6·5%; *M* in chloroform, 703. $C_{30}H_{48}O_2P_4W$ requires C, 48·1; H, 6·5%; *M*, 748·5).

trans-*Dicarbonyldi*-1,2-*bisdiphenylphosphinoethanechromium* (XXVI). Tricarbonylmesitylenechromium and the ditertiary phosphine (2 equiv.) were heated for 5 hr. at 190—195°. A slow nitrogen stream was passed through the fused mixture, which became deep red, and expelled mesitylene. Crystallisation of the cooled mass from toluene–light petroleum (b. p. 80—100°) gave a mixture of yellow and red crystals. This mixture was collected and washed with cold ethyl methyl ketone followed by a little cold toluene; only red crystals then remained (30%). These, when recrystallised as above, gave the trans-*dicarbonyl*, with one molecule of toluene of crystallisation, as very deep vermilion-red crystals, m. p. 279—280° (Found: C, 73·0; H, 5·8. $C_{54}H_{48}CrO_2P_4,C_7H_8$ requires C, 73·5; H, 5·7%). The compound was shaken repeatedly with portions of cold light petroleum (b. p. 40—60°), which removed toluene, leaving the trans-*dicarbonyl* as bright vermilion-red crystals, m. p. 279—280° (Found: C, 72·3; H, 5·35%; *M* in benzene, 1005. $C_{54}H_{48}CrO_2P_4$ requires C, 71·7; H, 5·35%; *M*, 905). The dicarbonyl is soluble in hot chloroform, benzene, or toluene to give deep cherry-red solutions from which it crystallises, with associated solvent, on cooling. With other solvents it undergoes change to the *cis*-isomer with partial decomposition. The ethyl methyl ketone washings from the initial product were evaporated to dryness and chromatographed on alumina in benzene. The operation afforded the tetracarbonyl (XVI) (36% based on tricarbonylmesitylenechromium), m. p. 210—212·5°, unchanged on admixture with the authentic sample.

cis-*Dicarbonyldi*-1,2-*bisdiphenylphosphinoethanechromium* (XXV). Methanol (12 ml.) was added to a solution of the *trans*-compound (0·25 g.) in warm chloroform (2·5 ml.). The colour immediately changed to pale orange, and the cis-*dicarbonyl* separated (0·165 g., 66%) (Found: C, 71·6; H, 5·7%); *M*, cryoscopic in 1,2-dibromoethane, 975). No further crop could be isolated from the mother-liquor. When the *cis*-compound is heated *in vacuo*, it slowly becomes red; it melts at 280—280·5° to a red liquid. The m. p. is unchanged on admixture with the

trans-compound. Cold solutions of the *cis*-compound in benzene or chloroform are orange, but when warmed they become deep red, and the *trans*-compound is deposited on cooling. The hot acetone solution is deep red-orange, but when cooled it becomes yellow-orange and deposits the pure *cis*-isomer.

cis-*Dicarbonyldi*-1,2-*bisdiphenylphosphinoethanemolybdenum*. A mixture of the tetracarbonyl (XVII) and the ditertiary phosphine (one equiv.) was heated at 210—220° for 60 hr. in an evacuated tube. The product, when recrystallised from benzene–methanol, gave the cis-*dicarbonyl* (XXVII) (72·5%), m. p. 324—325° (to a red liquid, reverting to a yellow solid on cooling) (Found: C, 68·75; H, 5·0%; *M*, 930. $C_{54}H_{48}MoO_2P_4$ requires C, 68·4; H, 5·1%; *M*, 949).

cis-*Dicarbonyldi*-1,2-*bisdiphenylphosphinoethanetungsten* (XXVIII). When this is prepared analogously to the molybdenum compound the yield is low. It is better obtained by heating the reactants in 1,2-dimethoxyethane under reflux in a nitrogen atmosphere, with strong ultraviolet illumination, for 35 hr. (silica flask). From the cooled mixture the *dicarbonyl* (47%) crystallised as plates, m. p. 320—323° (to a red liquid) after recrystallisation from the same

TABLE 3.

Dipole moments.

$10^3\omega$	$\Delta\varepsilon/\omega$	$10^3\Delta n/\omega$	$-\Delta v/\omega$
Compound (X)			
2·229	15·537	—	—
3·121	15·503	—	—
28·35	—	9·64	—
41·38	—	9·49	—
6·978	—	—	0·387
7·438	—	—	0·336
Compound (XI)			
1·954	14·879	—	—
3·179	14·860	—	—
30·74	—	10·16	—
38·94	—	10·01	—
4·760	—	—	0·420
6·615	—	—	0·438
Compound (XII)			
2·924	13·830	—	—
2·954	13·878	—	—
48·88	—	9·28	—
78·00	—	9·13	—
3·715	—	—	0·538
7·005	—	—	0·500
Compound (XIX)			
4·352	5·90	—	—
3·562	2·771	—	—
3·396	2·772	—	—
14·59	—	7·59	—
22·51	—	7·53	—
8·552	—	—	0·374
9·242	—	—	0·314

$10^3\omega$	$\Delta\varepsilon/\omega$	$10^3\Delta n/\omega$	$-\Delta v/\omega$
Compound (XX)			
3·035	10·354	—	—
4·380	10·153	—	—
39·30	—	10·47	—
43·43	—	10·66	—
6·870	—	—	0·393
6·952	—	—	0·432
Compound (XXI)			
3·457	9·585	—	—
4·636	9·582	—	—
18·98	—	8·94	—
30·07	—	9·28	—
5·605	—	—	0·517
6·136	—	—	0·456
Compound (XXIII)			
1·573	7·383	—	—
24·28	—	13·55	—
29·70	—	13·70	—
3·306	—	—	0·363
5·846	—	—	0·359
Compound (XXIV)			
2·754	6·832	—	—
3·864	6·826	—	—
17·31	—	12·45	—
18·63	—	12·36	—
4·999	—	—	0·580
7·369	—	—	0·556

$10^3\omega$	$\Delta\varepsilon/\omega$	$10^3\Delta n/\omega$	$-\Delta v/\omega$
Compound (XXV)			
0·9964	5·482	—	—
1·049	5·492	—	(0·35)
0·9964	3·645	—	—
1·049	3·699	—	(0·35)
Compound (XXVI)			
1·642	0·976	—	—
1·773	0·971	—	(0·35)
1·642	2·915	—	—
1·773	2·883	—	—
4·123	2·894	—	(0·35)
Compound (XXVII)			
0·9094	5·213	—	—
0·9102	5·242	—	(0·40)
Compound (XXVIII)			
1·050	5·511	—	—
1·160	5·504	—	(0·54)
Compound (XXIX)			
2·076	5·847	—	—
2·705	5·926	—	(0·35)
2·076	4·266	—	—
2·705	4·237	—	(0·35)
Compound (XXXIII)			
1·253	10·86	—	—
1·582	10·99	—	(0·32)

Compd.	$_TP$	$_EP$	$_OP$
X	1321	118	1185
XI	1394	123	1252
XII	1539	129	1390
XIX	670·5	137·2	512·7
	377·8	137·2	220·0
XX	1162	148	992

Compd.	$_TP$	$_EP$	$_OP$
XXI	1258	153	1082
XXIII	1073	202	841
XXIV	1092	179	886
XXV	1149*	(314)	789*
	840	(314)	479*
XXVI	380*	(314)	19*†
	708*	(314)	347*

Compd.	$_TP$	$_EP$	$_OP$
XXVII	1145*	(318)	779*
XXVIII	1262*	(295)	922*
XXIX	1180*	(265)	875*
	910*	(265)	605*
XXXIII	1854*	(248)	1568*

solvent (Found: C, 62·5; H, 4·85%; *M* in chloroform, 979. $C_{54}H_{48}O_2P_4W$ requires C, 62·6; H, 4·7%; *M*, 1037). The dicarbonyl derivatives of molybdenum and tungsten give pale orange solutions in hot benzene or chloroform. No indication of the existence of *trans*-isomers has been observed.

cis-*Dicarbonyldi(bisdiphenylphosphinomethane)chromium* (XXIX). This was prepared in the same way as the corresponding compound (XXV). The cooled reaction mixture, when crystallised from toluene–light petroleum (b. p. 80—100°), gave the cis-*dicarbonyl* (26%), m. p. 289° after recrystallisation from benzene under nitrogen followed by washing of the platy crystals by light petroleum (b. p. 40—60°) (they rapidly effloresced) (Found: C, 71·1; H, 5·2%; *M* in benzene, 918. $C_{53}H_{44}CrO_2P_4$ requires C, 71·2; H, 5·1%; *M*, 877). The solid is stable to air, but in solution the substance is oxidised, depositing a pale green sludge. Although solutions in chloroform or benzene become deep red-orange when warmed, the change is reversible, and no *trans*-isomer has been isolated.

Tritertiary Phosphine Complexes.—These were prepared in the same way as the tetracarbonyl derivatives, by heating the metal carbonyl and the phosphine in a sealed evacuated tube.

Tricarbonylbis-(o-diethylphosphinophenyl)phenylphosphinemolybdenum (XXX) was obtained from the hexacarbonyl and the triphosphine (2 equiv.) at 150° for 10 hr., then at 210° for 56 hr. The product was chromatographed in benzene on alumina; triphosphine followed by the tricarbonyl (68%), very pale yellow crystals from benzene–methanol, were eluted (Found: C, 56·5; H, 5·4. $C_{29}H_{33}MoO_3P_3$ requires C, 56·3; H, 5·4%).

Tricarbonylbis-(2-diphenylphosphinoethane)phenylphosphinemolybdenum (XXXI) was obtained from the carbonyl and triphosphine (one equivalent) at 150° for 15 hr. Recrystallisation from toluene gave the *tricarbonyl*, with one molecule of toluene of crystallisation (64%), as pale cream crystals, m. p. 265° (prior shrinking) (Found: C, 65·7; H, 4·8. $C_{37}H_{39}MoO_3P_3,C_7H_8$ requires C, 65·5; H, 5·1%). The unsolvated *tricarbonyl* was obtained as colourless crystals, m. p. 261·5—263° (much prior shrinking), from chloroform (Found: C, 62·5; H, 4·7. $C_{37}H_{33}MoO_3P_3$ requires C, 62·2; H, 4·7%).

Tricarbonyltris(diphenylphosphinomethyl)ethanechromium (XXXII). This was prepared from equimolar proportions of the reactants at 150° for 50 hr. (much of the chromium carbonyl was unchanged when the mixture was heated at 140° for 24 hr.). Recrystallisation from chloroform–light petroleum (b. p. 80—100°) gave the *tricarbonyl* (62%), m. p. 362° (prior decomp.) (Found: C, 68·8; H, 5·3. $C_{44}H_{39}CrO_3P_3$ requires C, 69·5; H, 5·2%).

Tricarbonyltris(diphenylphosphinomethyl)ethanemolybdenum (XXXIII) (prepared as above at 150° for 15 hr.). Recrystallisation from chloroform gave the *tricarbonyl* (49%) (Found: C, 65·8; H, 5·2. $C_{44}H_{39}MoO_3P_3$ requires C, 65·7; H, 4·9%).

Tricarbonyltris(diphenylphosphinomethyl)ethanetungsten (XXXIV). Preparations as above at 150° for 50 hr. gave the colourless *tricarbonyl* (38%), m. p. >400° (prior decomposition at 370°) (Found: C, 59·8; H, 4·6. $C_{44}H_{39}O_3P_3W$ requires C, 59·2; H, 4·4%).

Attempts to effect Further Replacement.—In attempts to effect complete expulsion of carbon monoxide and thus gain the compounds below, the dicarbonyl was heated with one equiv. or an excess of its constituent ditertiary phosphine. In all experiments there was no evidence of reaction, and the original components were recovered from the following experiments: $[Cr\{C_2H_4(PPh_2)_2\}_3]$, 50 hr., 195°.* $[Mo\{C_2H_4(PPh_2)_2\}_3]$, in decalin at reflux, 14 hr.; †‡ 60 hr., with an added 0·2 mole of $[Ni(CO)_2C_2H_4(PPh_2)_2]$.* $[W\{C_2H_4(PPh_2)_2\}_3]$, 330 hr., 225°.*

The tetracarbonyl (XVII) and the tritertiary phosphine (VI) (one equiv.) were heated *in vacuo* for 50 hr. at 210°, whereupon the tricarbonyl (XXXIII) (55%) (Found: C, 65·8; H, 4·9%) and the diphosphine (I; R = Ph) were formed. The dicarbonyl (XXVII) and the triphosphine (VI) did not react under these conditions.

Infrared Spectra.—These were measured on a Grubb–Parsons GS2A spectrometer.

Determination of Dipole Moments.—These were determined as described previously;[15] the same notations of measurements and estimated values have been used in Table 3.

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[*Received, May 26th,* 1961.]

* *In vacuo.* † Under nitrogen at atmospheric pressure. ‡ With strong ultraviolet illumination in a silica vessel.

[15] Chatt and Shaw, *J.*, 1959, 705.

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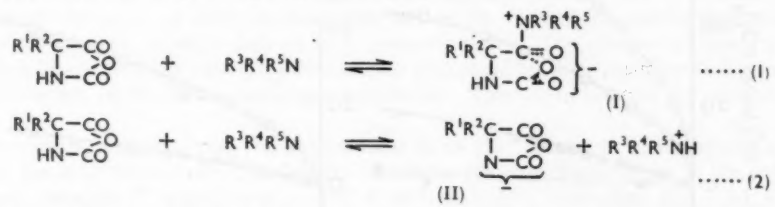
981. *The Initiation Step in the Polymerization of* N*-Carboxy-α-amino-acid Anhydrides. Part I. Catalysis by Tertiary Bases.*

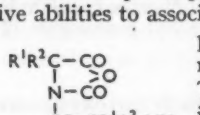
By C. H. Bamford and H. Block.

Observations on the polymerizations of *N*-carboxy-γ-ethyl-L-glutamate anhydride catalysed by pyridine, α-picoline, and 2,6-lutidine, and of *N*-carboxy-DL-phenylalanine anhydride catalysed by pyridine and 2,6-lutidine, show that the initial attack of the bases on the monomer molecule involves removal of the proton from the endocyclic NH group and not addition to a carbonyl group.

Investigations in these laboratories have shown that two mechanisms may be envisaged for the attack of a tertiary base on a *N*-carboxy-α-amino-acid anhydride molecule,[1,2,3] *viz.*, addition to the 5-carbonyl group (1) or removal of the proton from the endocyclic NH group (2). Either of the resulting intermediates (I) and (II) would be expected to react with a further molecule of monomer to give the bifunctional compound (III) which has been proposed as an intermediate in the polymerization of *N*-carboxy-α-amino-acid anhydrides initiated by tertiary and other aprotic bases.[1-4] Simple growth and cyclization involving (III) lead to the observed products, polypeptides, usually together with a small proportion of the corresponding 3-hydantoinylacetic acid.



It is desirable to distinguish between these alternative mechanisms of initiation. A similar problem arose in the interpretation of the mechanism of hydrolysis of carboxylic anhydrides catalysed by tertiary bases, and in this instance the elegant investigations of Gold and Jefferson [5] have shown that association with a carbonyl group is involved. The diagnostic technique employed involves the use of a series of tertiary bases having different relative abilities to associate with Lewis acids and to act as Brönsted bases. Since these processes are paralleled by those in equations (1) and (2) the mechanism may be inferred from the relative rates of reaction. Three suitable bases are pyridine, α-picoline, and 2,6-lutidine; it is known that their base strengths towards Brönsted acids increase in the order given, while their base strengths towards Lewis acids decrease in the order given.[6] The latter effect is attributable to steric shielding of the nitrogen lone pair by the α-methyl groups. We have used these bases, highly purified, to initiate the polymerizations of the *N*-carboxy-anhydrides of γ-ethyl-L-glutamate and DL-phenylalanine, and have thus been able to show unambiguously that the primary step in the polymerization is represented by (2). These findings should not be taken to indicate that (1) does not occur, but rather that, if this equilibrium is set up, it does not lead to further reaction at a significant rate.



(III)

[1] Ballard, Bamford, and Weymouth, *Nature*, 1954, **174**, 173.
[2] Ballard and Bamford, *J.*, 1956, 381.
[3] Bamford, Block, and Pugh, *J.*, 1961, 2057.
[4] Ballard, Bamford, and Weymouth, *Proc. Roy. Soc.*, 1955, *A*, **227**, 155.
[5] Gold and Jefferson, *J.*, 1953, 1409, 1416.
[6] Brown, Schlesinger, and Cordon, *J. Amer. Chem. Soc.*, 1942, **64**, 325; Brown and Barbaras, *ibid.*, 1947, **69**, 1137.

Experimental

Materials.—*N*-Carboxy-γ-ethyl-L-glutamate anhydride was prepared from γ-ethyl-L-glutamate kindly supplied by Dr. J. Watson. The *N*-benzyloxycarbonyl-derivative of this ester, prepared as described by Hanby *et al.*,[7] was cyclized by the use of thionyl chloride under the following standardized conditions. *N*-Benzyloxycarbonyl-γ-ethyl-L-glutamate was refluxed with thionyl chloride (20 ml.) for 12 min. in sodium-dried benzene (250 ml.). To the cooled mixture carbon tetrachloride (250 ml.) was added, followed, after crystallization, by light petroleum (b. p. 60—80°) (500 ml.). After collection, the resulting anhydride was washed successively with carbon tetrachloride and light petroleum (b. p. 60—80°), then recrystallized from dry ethyl acetate until free from chloride. Finally the anhydride was molecularly distilled at 110°/$<10^{-4}$ mm.

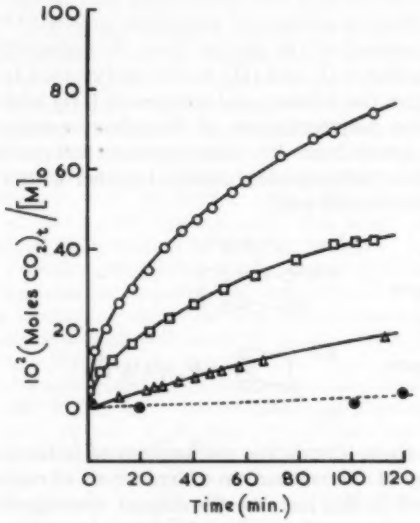


Fig. 1.

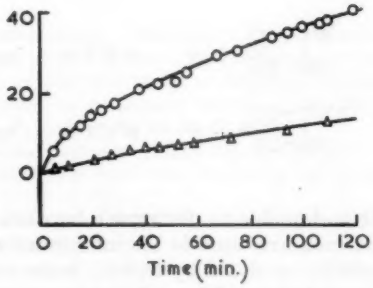


Fig. 2.

Fig. 1. Conversion–time curves for the polymerization of *N*-carboxy-γ-ethyl-L-glutamate anhydride (0·2 mole $l.^{-1}$) catalysed by pyridine and homologues (2·0 mole $l.^{-1}$) in *NN*-dimethylformamide at 25°:

△ pyridine, □ α-picoline, ○ 2,6-lutidine.

The broken curve shows a comparative experiment with *N*-carboxysarcosine anhydride (0·2 mole $l.^{-1}$) and 2,6-lutidine (2·0 mole $l.^{-1}$).

Fig. 2. Conversion–time curves for the polymerization of *N*-carboxy-DL-phenylalanine anhydride (0·2 mole $l.^{-1}$) catalysed by pyridine and 2,6-lutidine (2·0 mole $l.^{-1}$) in nitrobenzene at 25°:

△ pyridine, ○ 2,6-lutidine.

N-Carboxy-DL-phenylalanine anhydride[8] was purified by recrystallization from ethyl acetate–benzene until free from chloride. Immediately before use it was sublimed at $<10^{-4}$ mm.

N-Carboxysarcosine anhydride was prepared by the general method of Hanby *et al.*[3] and purified as described by Ballard *et al.*[4]

Pyridine, α-picoline, and 2,6-lutidine were purified by using vapour-phase chromatography.

[7] Hanby, Waley, and Watson, *J.*, 1950, 3239.
[8] Cf. *e.g.*, Hanby, Waley, and Watson, *J.*, 1950, 3009; Coleman, *J.*, 1950, 3222.

A 180 cm. column of " polyethylene glycol-400 " (Shell Chemical Co., Ltd.) (5%) on " Embacel " (May & Baker Ltd.) at 100° was used, argon being the carrier gas. The purity of individual cuts was confirmed by refractionation and in some cases by refractive-index measurements; *e.g.*, found for 2,6-lutidine n_D^{25} 1·4950 (lit.,[9] 1·4953).

Nitrobenzene and *NN*-dimethylformamide were purified as described in refs. 2 and 3, respectively.

Purified materials were handled exclusively in a dry box.

Method.—Polymerization is accompanied by the evolution of carbon dioxide, measurement of which provides a convenient way of following the reaction. For this purpose solutions of the monomer and base were placed in separate limbs of the reaction vessel described previously [3] connected to a constant-volume manometric system. Kinetic experiments were carried out in a thermostat at 25°.

Results and Discussion

Figs. 1 and 2 show typical conversion–time curves for the polymerizations at 25° of *N*-carboxy-γ-ethyl-L-glutamate anhydride in *NN*-dimethylformamide and *N*-carboxy-DL-phenylalanine anhydride in nitrobenzene. The bases show the same order of increasing reactivity towards both anhydrides, *viz.*, pyridine < α-picoline < 2,6-lutidine. Clearly the presence of traces of impurities could vitiate these observations. Normal purification techniques may not be adequate if the impurities include strong tertiary bases, which if present at a concentration of 0·015% (molar) in the catalysts could lead to initial rates of reaction of the order of 10% of those observed. The method of purification adopted ensures the absence of impurities at such concentrations. The absence of primary and secondary bases from the initiator solutions was confirmed by their inability to induce the polymerization of *N*-carboxysarcosine anhydride. This is illustrated for 2,6-lutidine in Fig. 1.

For reasons already given, the observations show that the major initial attack of the base on the anhydride involves ionization [equation (2)] since the rates are in the order of the base strengths [10] (pyridine $K_B = 1{\cdot}7 \times 10^{-9}$ mole l.$^{-1}$; α-picoline $K_B = 9{\cdot}1 \times 10^{-9}$ mole l.$^{-1}$; 2,6-lutidine $K_B = 4{\cdot}2 \times 10^{-8}$ mole l.$^{-1}$). Addition at a carbonyl group cannot be a rate-determining step, nor can an adduct such as (I) formed in a pre-equilibrium be involved, since both the rate of addition and the equilibrium concentration of (I) would be affected by the stereochemistry of the base. As a result the rates of reaction would be in the reverse order to that found. The possibilities that equilibrium (1) is established and even that (I) is responsible for a minor part of the reaction cannot be excluded.

These observations and conclusions contrast markedly with those appertaining to the catalysed hydrolysis of carboxylic anhydrides.[5]

We thank Mr. D. R. Boreham and Mrs. D. Kapur for assistance with the experimental work.

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[*Received, June 2nd,* 1961.]

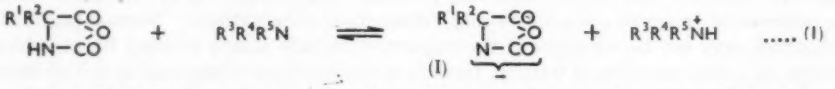
[9] Brown, Johnson, and Podall, *J. Amer. Chem. Soc.*, 1954, **76**, 5556.
[10] Gero and Markham, *J. Org. Chem.*, 1951, **16**, 1835.

982. *The Initiation Step in the Polymerization of N-Carboxy-α-amino-acid Anhydrides. Part II.*[1] *Effects Related to the Structure of Amine Initiators.*

By C. H. Bamford and H. Block.

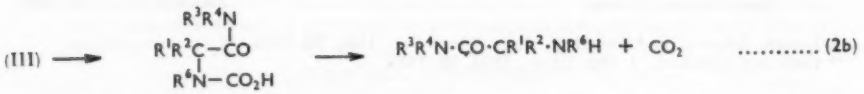
It is shown that the interaction of *N*-carboxy-α-amino-acid anhydrides with primary and secondary bases is not confined to the conventional mechanism involving addition to the 5-carbonyl group in the anhydride molecule. A reaction of the tertiary-base type may also occur, following removal of the proton of the endocyclic NH group; this reaction is fast and leads to polymers with molecular weights greater than expected; it is favoured by steric shielding of the lone pair in the initiator molecule and a high base strength.

In Part I [1] we have shown that the initiation of polymerization of *N*-carboxy-α-amino-acid anhydrides by tertiary bases involves the primary removal of the proton attached to the endocyclic nitrogen atom:



Previous studies [1-3] have indicated that this is followed by attack of the resulting ion (I) on the 5-carbonyl group of a second molecule of anhydride to form a bifunctional intermediate (IIa) which, by propagation and coupling reactions, may achieve the structure (IIb). Primary and secondary amines can initiate polymerization by direct addition to the 5-carbonyl group of the oxazolidine-2,5-dione ring,[4] as shown in schemes

(2a and b). If R^6 is not hydrogen, reactions (2a) and (2b) constitute the sole initiation processes with primary and secondary amines. (Addition to the 2-carbonyl group, which occurs much less readily, cannot be regarded as an initiation step.) Tertiary bases do not



react with such anhydrides [2,3] since reaction (2b) cannot occur, but this does not exclude the possibility of an equilibrium similar to (2a) being established.

We show in this paper that if the anhydride and initiator have the requisite protons

[1] Part I, Bamford and Block, preceding paper.
[2] Ballard, Bamford, and Weymouth, *Nature*, 1954, **174**, 173; Ballard and Bamford, *J.*, 1956, 381.
[3] Bamford, Block, and Pugh, *J.*, 1961, 2057.
[4] See, *e.g.*, Bamford, Elliott, and Hanby, "Synthetic Polypeptides," Academic Press, Inc., New York, 1956; Katchalski and Sela, *Adv. Protein Chem.*, 1958, **13**, 243; Bamford and Block, Symposium on Poly-α-amino-acids, University of Wisconsin, 1961.

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both reactions (1) and (2) can take place simultaneously, resulting in rates of reaction and polymer sizes inexplicable in terms of the mechanism (2) alone.

The extent to which these reactions deviate from the conventional scheme depends on the relative contributions of (1) and (2) to the polymerization, which, as discussed below, are determined by the strength and stereochemistry of the initiating base.

Experimental

Materials.—*N*-Carboxysarcosine anhydride, prepared by the general method of Hanby *et al.*,[5] was sublimed at 100°/10^{-4} mm.

N-Carboxy-γ-ethyl-L-glutamate anhydride was prepared and purified as described in Part I.[1]

Di-isopropylamine and n-hexylamine were kept over solid sodium hydroxide and then fractionated. This process was repeated twice.

NN-Dimethylformamide was purified as described in ref. 3.

Purified materials were handled exclusively in a dry-box.

Methods.—The rates of polymerization of *N*-carboxy-γ-ethyl-L-glutamate anhydride in *NN*-dimethylformamide were determined by measurement of the carbon dioxide evolved, using the constant volume technique described previously.[3] Since carbon dioxide catalyses[6] the polymerization of *N*-carboxysarcosine anhydride the rate of reaction of this anhydride with n-hexylamine was measured under effectively zero carbon dioxide pressure in an apparatus to be described later. The reaction with di-isopropylamine was followed in the constant-volume apparatus; it is so slow that for present purposes catalysis by carbon dioxide is irrelevant.

Reduced viscosities of the resulting poly-γ-ethyl-L-glutamate specimens at 0·5% concentration (w/v) were determined in dichloroacetic–trifluoroacetic acid (9 : 1 v/v) at 25°. For this purpose the polymers prepared by di-isopropylamine initiation were precipitated from the reaction mixture with ether. The polymers obtained from n-hexylamine initiation under the conditions used could not be precipitated satisfactorily. The solvent was therefore evaporated in a vacuum at room temperatures, and the polymer redissolved in chloroform and cast into a film.

Results and Discussion

The Figure shows typical conversion–time curves for the polymerization at 25° of the two anhydrides initiated by di-isopropylamine. In the case of *N*-carboxysarcosine anhydride the reaction is slow initially but accelerates, the conversion–time curve becoming almost linear. The first step in this reaction is therefore slower than the subsequent propagation. This arises from the conversion of the slowly reacting di-isopropylamine into the more reactive base group of polysarcosine.[4] On the other hand, the reaction of *N*-carboxy-γ-ethyl-L-glutamate anhydride with di-isopropylamine is remarkably rapid, and the yield of carbon dioxide is less than 100%. However, these two anhydrides have approximately the same reactivity towards n-hexylamine, the conversion–time curves lying close together and between those for di-isopropylamine initiation.

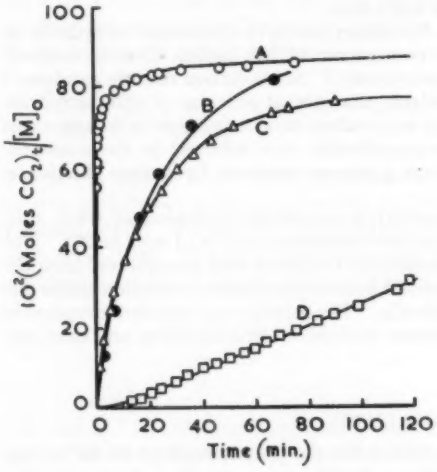
Di-isopropylamine is a strong base[7] ($K_B = 1{\cdot}1 \times 10^{-3}$ mole $l.^{-1}$) and we believe that its low rate of reaction with *N*-carboxysarcosine anhydride is due to steric hindrance encountered during addition to the 5-carbonyl group of the anhydride [equation (2a)]. On this basis the high reactivity of di-isopropylamine towards *N*-carboxy-γ-ethyl-L-glutamate anhydride must indicate a different mode of initiation, which we identify with ionization according to equation (1), the primary step in the tertiary base-catalysed polymerization.

Support for this is provided by measurements of the reduced viscosity of the polymers.

[5] Hanby, Waley, and Watson, *J.*, 1950, 3009.
[6] Ballard and Bamford, *Proc. Roy. Soc.*, 1954, *A*, **223**, 495.
[7] Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469.

The values obtained for poly-γ-ethyl-L-glutamate were 6·12 and 1·46 base mole^{-1} l. for initiation of the polymerization by di-isopropylamine and n-hexylamine respectively. In each case the initial ratio [anhydride] : [initiator] was 15 : 1. Comparison with the results of Doty *et al.*[8] on the molecular weights and intrinsic viscosities of poly-γ-benzyl-L-glutamate gives lower limits of the degrees of polymerization in our cases of 150 and 60 for di-isopropylamine and n-hexylamine, respectively. Similar observations have been reported by Blout and Karlson [9] for the polymerization of *N*-carboxy-γ-benzyl-L-glutamate anhydride initiated by diethylamine and n-hexylamine. The observation that one can obtain polymers with degrees of polymerization greatly in excess of the ratio [anhydride] : [initiator] must be interpreted in terms of a contribution to the reaction by the tertiary-base mechanism. It is known [2,4] that this type of reaction can readily lead to degrees of polymerization greater than the [anhydride] : [initiator] ratio.

If both modes of polymerization [initial steps (1) and (2)] occur together interaction between them will take place during propagation. The bifunctional intermediates (IIa and IIb), in addition to growing at both ends and coupling together as in the normal tertiary base mechanism,[1-3] can also react with the initiator or the terminal base group of a monofunctional chain which arises from initiation according to equation (2). It is thus conceivable that every polymer molecule should carry an initiator fragment as a terminal group, and that the number-average degree of polymerization would be given by the [anhydride] : [initiator] ratio. This is by no means necessary; some chains may be terminated as in the tertiary base-catalysed polymerization (*e.g.*, by cyclization) or there may be unchanged initiator at the end of the reaction. In all cases it is to be expected that the molecular distribution would be broader than that calculated for a polymerization based on (2) above (*i.e.*, a Poisson distribution [4]). The weight average and also the viscosity-average degrees of polymerization may therefore be considerably higher than expected, as is found in the above examples.



Conversion–time curves for polymerization of *N*-carboxy-α-amino-acid anhydrides (concn. 0·224 mole l.$^{-1}$) initiated by amines (concn. 0·015 mole l.$^{-1}$) at 25° in *NN*-dimethylformamide solution.

A, *N*-Carboxy-γ-ethyl-L-glutamate anhydride–di-isopropylamine; B, *N*-carboxysarcosine anhydride–n-hexylamine; C, *N*-carboxy-γ-ethyl-L-glutamate anhydride–n-hexylamine; D, *N*-carboxysarcosine anhydride–di-isopropylamine.

It is apparent that the stereochemistry of the initiating base has a marked effect on the relative importance of reactions 1 and 2, increasing hindrance favouring 1. We believe that the base strength of the initiator will also influence the course of reaction. The concentrations of the intermediate (I), with a series of amines, will be proportional to the square roots of the base strengths. Although in the absence of steric complications

[8] Doty, Bradbury, and Holtzer, *J. Amer. Chem. Soc.*, 1956, **78**, 947.
[9] Blout and Karlson, *J. Amer. Chem. Soc.*, 1956, **78**, 941.

the association (2a) might appear to depend entirely on base strength, this is not so since the structure (III) really represents a series of tautomers in which the proton may be situated on any of the oxygen atoms. The energy decrease in the tautomerization would be expected to be an inverse function of the base strength. As a result the equilibrium (2a) is less dependent on base strength than is equilibrium (1). Thus, steric considerations apart, the stronger the initiating base, the greater the relative importance of the tertiary base type of initiation (1). These conclusions may be applied to the polymerizations of *N*-carboxy-α-amino-acid anhydrides initiated by preformed polymers, which are known experimentally to be of the first order in anhydride concentration.[4] In these circumstances the base is comparatively weak, so that initiation by (2) is favoured. The complete absence of initiation by (1) cannot be inferred since a minor portion of a tertiary-base type mechanism may not be detectable kinetically.

We thank Mr. D. R. Boreham and Mrs. D. Kapur for assistance with the experimental work.

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983. *Constituents of the Higher Fungi. Part I. Hispidin, A New 4-Hydroxy-6-styryl-2-pyrone from* Polyporus hispidus *(Bull.) Fr.*

By R. L. EDWARDS, D. G. LEWIS, and D. V. WILSON.

The isolation of a new 6-(3,4-dihydroxystyryl)-4-hydroxypyrone from *Polyporus hispidus* is described. Properties and reactions of this compound leading to assignment of its structure (I; R = OH) are described. The structure has been verified by synthesis of the derived trimethyl ether.

THE basidiomycete *Polyporus hispidus* (Bull.) Fr., parasitic chiefly on ash (*Fraxinus excelsior*), produces considerable quantities of yellow-brown colouring matters in its bracket-shaped sporophore. Zopf [1] isolated several yellow amorphous materials from the fungus but only described colour reactions. Zellner [2] reported similar amorphous materials. Robertson and his co-workers [3] obtained eburicoic acid from the mycelium of the fungus grown in culture, but did not investigate any pigments.

In this laboratory *Polyporus hispidus* collected from ash has yielded a yellow crystalline, optically inactive metabolite, which we name hispidin. The yield varied from different batches of fungi; actively growing, small fruiting bodies provide a cleaner product in greater quantity than do the dark mature specimens.

The pigment, when purified by crystallisation from ethanol or through one of the acetates, has the formula $C_{13}H_{12}O_6$, contains no methoxyl or *C*-Me group, is not reduced by sodium dithionite or sulphur dioxide, and does not give Craven's reaction [4] or colour tests with indole or ethylenediamine (for benzoquinones and naphthaquinones [5]). It yields an olive-green colour with ferric chloride, and reduces silver nitrate and Fehling's solution, but gives no precipitate with Brady's reagent. It yields no colour with magnesium and hydrochloric acid (flavones and flavanols), gives a negative Gibbs test and is insoluble in dilute acids, but dissolves in concentrated sulphuric acid to a yellow and in 2N-sodium hydroxide to an orange-yellow solution.

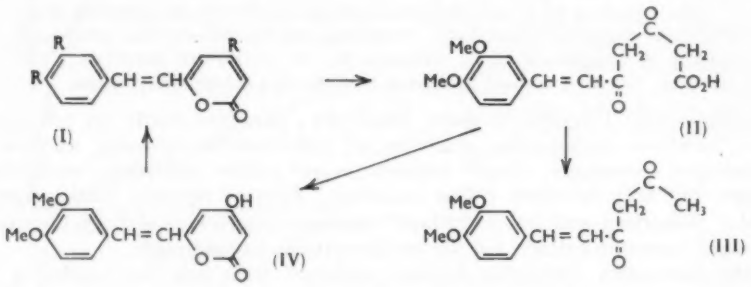
With acetic anhydride hispidin yields (*a*) di-*O*-acetylhispidin, $C_{17}H_{14}O_7$, slowly dissolving in cold sodium hydrogen carbonate to a yellow solution, (*b*) tri-*O*-acetylhispidin, $C_{19}H_{16}O_8$, insoluble in sodium bicarbonate solution, readily formed from the diacetate, and hydrolysed

[1] Zopf, *Bot. Z.*, 1889, **47**, 53.
[2] Zellner, *Monatsh.*, 1920, **41**, 443.
[3] Cort, Gascoigne, Holker, Ralph, Robertson, and Simes, *J.*, 1954, 3721.
[4] Craven, *J.*, 1931, 1605.
[5] Karius and Mapstone, *Chem. and Ind.*, 1956, 266; Bu'Lock and Harley-Mason, *J.*, 1951, 703.

to the diacetate by boiling alcohol, and (*c*) a pale yellow compound $C_{21}H_{18}O_9$ containing one *C*- and three *O*-acetyl groups insoluble in sodium hydrogen carbonate solution but dissolving slowly in 2N-sodium hydroxide to an orange solution, and giving a precipitate with Brady's reagent. With dimethyl sulphate, hispidin yields a yellow and a colourless trimethyl ether, both $C_{16}H_{16}O_5$; diazomethane gives only the yellow ether (the relationship between these two ethers has not been established; they give similar infrared spectra). Di-*O*-acetylhispidin reacts readily with diazomethane, to yield a compound, $C_{18}H_{16}O_7$, which is readily hydrolysed to *O*-methylhispidin which with diazomethane yields the yellow tri-*O*-methylhispidin. The formulæ of these derivatives suggest that the pigment is hydrated.

Chromic acid oxidises di-*O*-acetylhispidin to protocatechuic acid diacetate; protocatechualdehyde diacetate is produced by ozonolysis of tri-*O*-acetylhispidin, indicating that a catechol nucleus is present but not included in a fused ring system.

The ultraviolet spectrum of hispidin is similar to the spectra of certain unsaturated ketones.[6] The high-intensity band at 3730 Å suggests the presence of a carbonyl group conjugated *via* several double bonds to a benzene ring, and since hispidin does not show ketonic properties the carbonyl group is presumably present in a cyclic structure (*e.g.*, a lactone or a pyrone). Hispidin has a strong infrared band at 3392 cm.$^{-1}$, with broad but less intense absorption at 2564 cm.$^{-1}$ characteristic of strongly chelated phenols.[7] Intense absorption also occurs at 1684 and 1661 cm.$^{-1}$, at first identified with the carbonyl stretching vibration of a strongly chelated aromatic acid; however, no chemical evidence for the existence of such a group could be obtained. Strong absorption by di-*O*-acetyl-



hispidin at 2914 cm.$^{-1}$ confirms the presence of a free hydroxyl group, but the absorption at 1684 cm.$^{-1}$ in the spectrum of hispidin has been replaced by bands at 1757 and 1706 cm.$^{-1}$. The higher-frequency band is in the position appropriate for a phenolic acetate group. Tri-*O*-acetylhispidin, $C_{19}H_{16}O_8$, shows no absorption at 2941 cm.$^{-1}$ but intense absorption at 1757 and 1715 cm.$^{-1}$. The carbonyl absorption band in the derivatives of hispidin is at a higher wavelength than that normally associated with β-, γ-, or δ-lactones. Randall *et al.*[8] quote 1721 cm.$^{-1}$ for the carbonyl absorption of dehydroacetic acid, but Bellamy[9] notes complex interactions for lactones with two carbonyl groups in the same six-membered ring.

Naturally occurring 6-substituted 2-pyrones include yangonin[10] [(I; R = OMe) but without the 3'-methoxy-group], anibine,[11] and 5,6-dehydrokawain;[11] methysticin,[10]

[6] Wilds, Beck, Close, Djerassi, Johnson, and Shunk, *J. Amer. Chem. Soc.*, 1947, **69**, 1984.
[7] Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen, London, 2nd edn. 1958, pp. 99—105.
[8] Randall, Fowler, Fuson, and Dangle, "Infra-red Determination of Organic Structures," Van Norstrand, Princeton, 1949, p. 231.
[9] Bellamy, ref. 7, p. 186.
[10] Borsche and Lewinsohn, *Ber.*, 1933, **66**, 1792 and references therein.
[11] Gottlieb and Mors, *J. Org. Chem.*, 1959, **24**, 17; Gottlieb, Mors, and Djerassi, *J. Amer. Chem. Soc.*, 1957, **79**, 4507.

marindinin,[12] and kawain [10] are similar 5,6-dihydro-2-pyrones. Several of them have been differentiated spectroscopically [13] from the 4-pyrone isomers: the carbonyl absorption of methoxy-2-pyrones occurs at 1724—1709 cm.$^{-1}$ and of 4-pyrones at ~1667 cm.$^{-1}$.

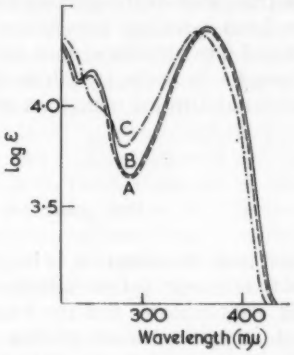


FIG. 1. Ultraviolet absorption spectra of tri-*O*-methylhispidin [(A) from hispidin, (B) synthetic] and (C) yangonin.

The infrared similarities were re-inforced when it was found that yangonin has an ultraviolet absorption peak at 3600 Å and tri-*O*-methylhispidin one at 3660 Å (cf. Fig. 1). The position of this maximum suggests that this latter is 6-(3,4-dimethoxystyryl)-4-methoxy-2-pyrone (I; R= OMe): the isomeric 4-pyrone would be expected to absorb at about ~3500 Å (cf. pseudoyangonin 3450 Å). Presumably the bathochromic shift of 60 Å is due to the additional methoxy-group in the benzene ring. This formulation is supported

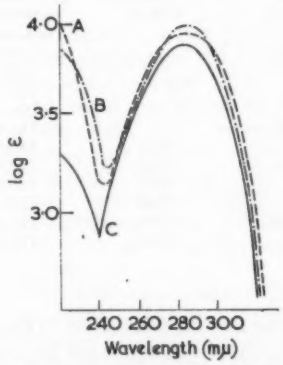


FIG. 2. Ultraviolet absorption spectra of (A) di-*O*-acetyldihydrohispidin, (B) dihydrohispidin, and (C) compound (V; R = H).

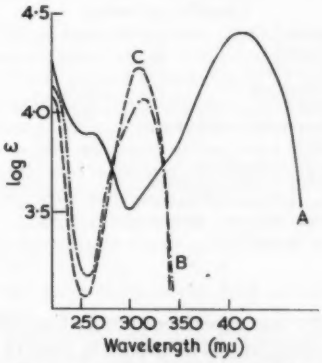


FIG. 3. Ultraviolet absorption spectra of (A) 3-acetylhispidin, (B) 3-acetyldihydrohispidin, and (C) dehydroacetic acid (V; R = Ac).

by the results of alkaline degradation. Tri-*O*-methylhispidin resembles yangonin and the constituents of the rosewoods (*Aniba* species) in that the ring is opened with simultaneous removal of the 4-methoxy-group. The unsaturated keto-acid (II) readily lost carbon dioxide on warming to produce the diketone (III) and was recyclised with acetic anhydride to the 4-hydroxy-2-pyrone (IV). The identity of the last compound was confirmed by methylation to tri-*O*-methylhispidin with diazomethane.

[12] Van Veen, *Rec. Trav. chim.*, 1939, **58**, 521.

[13] Chmielewska, Cieslak, Gorezynska, Kontnik, and Pitakowska, *Tetrahedron*, 1958, **4**, 36; Herbst, Mors, Gottlieb, and Djerassi, *J. Amer. Chem. Soc.*, 1959, **81**, 2427; Bu'Lock and Smith, *J.*, 1960, 502.

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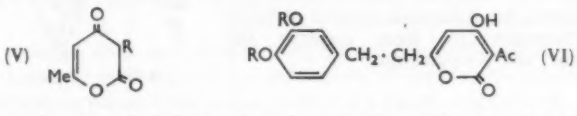
On the above evidence we formulate hispidin as 4-hydroxy-6-(3,4-dihydroxystyryl)-2-pyrone (I; R = OH). Di-*O*-acetylhispidin is the 3′,4′-diacetate, the yellow triacetate is the 4,3′,4′-derivative, and *O*-methylhispidin is the 4-methyl ether.

3,4-Dihydro-6-methylpyran-2,4-dione (triacetic lactone) (V; R = H) is readily *C*-acetylated, yielding dehydroacetic acid [14] (V; R = Ac). The fourth acetyl group introduced into hispidin or into tri-*O*-acetylhispidin by use of the boron trifluoride–acetic acid complex in acetic anhydride is similarly considered to be a 3-*C*-acetyl group. The ultraviolet absorption maximum at 4100 Å supports this formulation. 3-Acetylhispidin,



obtained from its triacetate, is bright red and sparingly soluble in polar solvents in which it yields intensely yellow solutions showing a faint green fluorescence. Benzoylation yielded a dibenzoate, and the triacetate was re-formed by acetylation. With dimethyl sulphate it gave a trimethyl ether; with methyl iodide it gave the same trimethyl ether and the 3′,4′-dimethyl ether, the latter soluble in warm aqueous sodium hydroxide but not amenable to acetylation. The infrared spectra of 3-acetylhispidin and its derivatives show a new band, above 1666 cm.$^{-1}$, corresponding to the new reactive carbonyl group (see Table).

TABLE 1.

Infrared absorption bands (cm.$^{-1}$) of hispidin and its derivatives.

Hispidin derivative	C=O of OAc	C=O of 3-Ac	C=O of pyrone
(Hispidin)			1684, 1661
Di-*O*-acetyl	1757		1706
Tri-*O*-acetyl	1757		1715
Tri-*O*-methyl			1701
O-Methyl			1664
Di-*O*-acetyl-*O*-methyl	1752		1715
3-Acetyl		1712	1686
3-Acetyl, triacetate	1776	1736	1729
3-Acetyl, trimethyl ether		1724	1701
3-Acetyl, dimethyl ether		1733	1718
3-Acetyl dihydro, diacetate	1758i	1733	1715
3-Acetyl dihydro		1724i	1704

i = Inflexion.

Difficulty was experienced in hydrogenating hispidin and its derivatives in the presence of Adams catalyst. The products were in most cases oils which could not be crystallised. However, 3-acetylhispidin triacetate and dimethyl ether gave crystalline dihydro-compounds (VI; R = Ac and Me respectively). The removal of an *O*-acetyl group from the former is comparable with the removal of an *O*-acetyl group from acetylyanganolactone on hydrogenation.[15] The identity of these products was established by their ultraviolet absorption spectra (cf. Fig. 2); both show an intense peak at 3100 Å, similar to that [16] of dehydroacetic acid (V; R = Ac) and in accord with the observations by Borsche and his co-workers [10] that the double bond between the two rings in yangonin is preferentially reduced on catalytic hydrogenation. Di-*O*-acetylhispidin was hydrogenated over palladium–charcoal to the above-mentioned crystalline dihydro-derivative which was readily hydrolysed to dihydrohispidin. Both these compounds have an ultraviolet absorption maximum at 2850 Å [cf. (V; R = H) [16] at 2830 Å (see Fig. 3)].

[14] Collie, *J.*, 1900, **77**, 976.
[15] Borsche and Bodenstein, *Ber.*, 1929, **62**, 2513.
[16] Berson, *J. Amer. Chem. Soc.*, 1952, **74**, 5172.

From the position of the pyrone carbonyl band in the infrared spectra of hispidin, *O*-methylhispidin, and 3-acetylhispidin it appears at first sight that these compounds exist preferentially as the 4-pyrone isomers in the solid state. In alcohol, as revealed by the ultraviolet spectra, these compounds exist as the 2-pyrones. The acetates seem to exist as 2-pyrones both in the solid state and in solution. Similar observations have been made by Herbst *et al.*;[13] hydroxy-6-phenylpyrone has been observed to exist as the 4-pyrone in the solid state and as the 2-pyrone in alcoholic solution. An explanation based on tautomerism is, however, difficult to reconcile with the infrared absorption of *O*-methylhispidin, which appears to exist as the 4-pyrone in the solid state and the 2-pyrone in alcohol ($\lambda_{max.}$ 3780 Å); this compound is prepared by the acid hydrolysis of di-*O*-acetyl-*O*-methylhispidin, which occurs as the 2-pyrone both in the solid state and in solution. Tautomerism is impossible for *O*-methylhispidin and we must assume that both it and its diacetate are 2-pyrones, the infrared pyrone carbonyl absorption being modified and moved to higher wavelength by intermolecular bonding. It is significant that this shift of absorption occurs only in those compounds in which the hydroxyl groups in the benzene ring are unsubstituted.

Bu'Lock and Smith[13] recently synthesised yangonin by an unambiguous method involving the condensation of *p*-methoxybenzaldehyde with the 4-methyl ether of compound (V). We carried out a similar synthesis with veratraldehyde in place of *p*-methoxybenzaldehyde: tri-*O*-methylhispidin, identical with that from hispidin, was obtained.

Experimental

Ultraviolet spectra were determined for alcohol solutions and infrared spectra for potassium bromide discs.

Isolation of Hispidin.—The fresh brownish-yellow sporophore was sliced and extracted (11 l. Soxhlet) with alcohol until the syphoning extract was pale yellow. 1 Litre of alcohol was used for six batches of fresh fungus. The extract (1 l.) was poured into water (5 l.) and set aside overnight. The solid was separated, dried, and extracted with benzene (Soxhlet) until the extract was colourless. The residue was extracted with acetone and the reddish-brown solution (450 ml.) concentrated to 100 ml. Ether (300 ml.) was added, and the yellowish-brown solid (A) (13 g.) which separated was filtered off and washed with ethyl acetate (3 × 150 ml.). The ethyl acetate washings were combined with the main filtrate; this led to the deposition of a further quantity of solid (B) (5 g.). The red filtrate was evaporated to 150 ml., then cooled for 2 hr. at 0° and the reddish-yellow precipitate (C) (6 g.) collected and washed with ethyl acetate (50 ml.).

Evaporation of the ethyl acetate solution to 75 ml. gave more yellow solid (D) (11 g.) when kept at 0° overnight. Each fraction was acetylated.

Fractions C and D (5 g.) were left overnight with acetic anhydride (50 ml.) and pyridine (10 ml.), then poured into water (500 ml.). The precipitate (7·6 g.) was extracted with benzene (2 × 50 ml.), and the yellow residue (2·9 g.) filtered off and crystallised three times from ethyl methyl ketone, to yield *di-O-acetylhispidin* as pale yellow needles, m. p. 227° [Found: C, 61·75; H, 4·2%; *M* (ebullioscopic in acetone), 311. $C_{17}H_{14}O_7$ requires C, 61·8; H, 4·2%; *M*, 330], $\lambda_{max.}$ 351, 255, and 234 mμ (log ε 4·40, 4·14, and 4·20).

The benzene mother-liquor was evaporated to 5 ml. and set aside for 12 hr. The yellow-brown solid (0·2 g.), crystallised once from benzene and twice from alcohol, gave pale yellow needles and plates of *tri-O-acetylhispidin*, m. p. 142—143° [Found: C, 61·5; H, 4·2%; *M* (*X*-ray), 368. $C_{19}H_{16}O_8$ requires C, 61·3; H, 4·3%); *M*, 372] $\lambda_{max.}$ 360, 269, 262, and 237 mμ (log ε 4·40, 4·10, 4·10, and 4·06).

Fractions A and B gave oils which yielded no crystalline material.

Tri-*O*-acetylhispidin (or di-*O*-acetylhispidin) (0·25 g.), ethanol (20 ml.) and 2N-sulphuric acid (20 ml.) were refluxed for 2 hr., then set aside at room temperature for 12 hr., and the yellow precipitate filtered off. Recrystallisation from aqueous alcohol yielded *hispidin* as yellow needles (0·7 g.), m. p. 259° (decomp.) (preheated block) [Found: C, 58·7; H, 4·7%; *M* (potentiometric titration), 260. $C_{13}H_{10}O_5,H_2O$ requires C, 59·1; H, 4·5%; *M*, 264], $\lambda_{max.}$

373 and 257 mμ (log ε 4·28 and 4·07), insoluble in light petroleum, sparingly soluble in hot chloroform or benzene, and very soluble in hot alcohol or acetone.

Occasionally, sporophores particularly rich in hispidin were encountered; material obtained from them on evaporation of the acetone solution crystallised from alcohol and aqueous alcohol to yield pure hispidin with much loss.

Acetyl Derivatives of Hispidin.—Hispidin (0·1 g.), acetic anhydride (2 ml.), and pyridine (1 drop) were set aside at room temperature for 8 hr., then poured into cold water (25 ml.). The benzene-soluble portion of the precipitate, when crystallised three times from methyl alcohol, yielded tri-*O*-acetylhispidin (0·08 g.) as golden-yellow needles, m. p. and mixed m. p. 142—143° (Found: C, 61·0; H, 4·3%).

Use of 1 ml. of pyridine led to a solid which, after extraction with cold benzene (10 ml.), recrystallised from ethyl methyl ketone to yield di-*O*-acetylhispidin (0·07 g.), m. p. and mixed m. p. 227° (Found: C, 61·8; H, 4·5%).

Tri-*O*-acetylhispidin (0·12 g.) was refluxed for 7 hr. with 95% ethanol (10 ml.), then evaporated; the residual solid recrystallised from ethyl methyl ketone to yield di-*O*-acetylhispidin (0·05 g.), m. p. and mixed m. p. 227°.

A suspension of di-*O*-acetylhispidin (0·5 g.) in ether (10 ml.) was treated with diazomethane (1·1 g. in 75 ml. of ether). After 5 hr. at room temperature the excess of diazomethane was destroyed by acetic acid. The solid (0·47 g.) was collected and recrystallised three times from methanol, to yield *di*-O-*acetyl*-O-*methylhispidin* as pale yellow needles, m. p. 205° (Found: C, 62·7; H, 4·8. $C_{18}H_{16}O_7$ requires C, 62·8; H, 4·65%), $\lambda_{max.}$ 346 and 255 mμ (log ε 4·40 and 4·12).

O-*Methylhispidin.*—Di-*O*-acetyl-*O*-methylhispidin (0·21 g.) was refluxed for 30 min. with 2N-sulphuric acid (6 ml.) and ethanol (6 ml.). The yellow solution deposited O-*methylhispidin* (0·14 g.) when left overnight. Crystallisation from glacial acetic acid yielded needles, m. p. 257° (decomp.) (preheated block) (Found: C, 64·7; H, 4·8. $C_{14}H_{12}O_5$ requires C, 64·6; H, 4·6%), $\lambda_{max.}$ 378, 255 mμ (log ε 4·26, 4·10). Acetylation of this product with acetic anhydride and a trace of pyridine for 15 hr. at 20° regenerated di-*O*-acetyl-*O*-methylhispidin, m. p. 205°, in almost quantitative yield.

Tri-O-*methylhispidin.*—(i) A mixture of hispidin (0·3 g.), acetone (15 ml.), potassium carbonate (6 g.), and dimethyl sulphate (3 ml.) was refluxed for 5 hr., then filtered and evaporated *in vacuo* to a red oil which rapidly solidified. This was shaken with 2N-sodium hydroxide (25 ml.) and filtered, yielding *tri*-O-*methylhispidin* (0·19 g.), m. p. 153—158°. After crystallising four times from methanol the compound was obtained as pale yellow needles, m. p. 164° [Found: C, 66·6; H, 5·4; *M* (ebullioscopic in acetone) 287, (mass spectroscopy) 288. $C_{16}H_{16}O_6$ requires C, 66·7; H, 5·6%); *M*, 288], $\lambda_{max.}$ 366 and 251 mμ (log ε 4·39 and 4·17). Evaporation of the mother-liquors from the recrystallisation gave needles (25 mg.) of an *isomer*, m. p. 197° (from ethyl acetate) (Found: C, 66·4; H, 5·8%), $\lambda_{max.}$ 266 mμ (log ε 4·21).

(ii) Hispidin (0·1 g.) was left with diazomethane (0·2 g.) in methanol (3 ml.) and ether (25 ml.) at room temperature for 1·5 hr., then treated with acetic acid and filtered [to remove the trimethyl ether (0·02 g.), m. p. 162°]. Evaporation gave an oil which solidified on trituration with water. Recrystallisation from aqueous alcohol and then from methanol yielded a further 0·03 g. of pure trimethyl ether.

(iii) *O*-Methylhispidin (0·05 g.) in methanol (2 ml.) and ether (10 ml.) with diazomethane (0·2 g.) (16 hr.) gave an oil which was dissolved in chloroform (10 ml.), washed with sodium hydrogen carbonate solution (10 ml.), dried (Na_2SO_4), and chromatographed on magnesium oxide (B.D.H. chromatographic grade). Elution with chloroform gave a fast-moving yellow band yielding tri-*O*-methylhispidin, m. p. and mixed m. p. 164°.

3-*Acetylhispidin Triacetate.*—Di-*O*-acetylhispidin (0·5 g.) in acetic anhydride (10 ml.) and boron trifluoride–acetic acid complex (5 drops) was heated on the water bath for 30 min., then poured into water. The solid was collected and recrystallised three times from alcohol, to yield 3-*acetylhispidin triacetate* as yellow needles (0·15 g.), m. p. 193—194° (decomp.) [Found: C, 61·1; H, 4·45%; *M* (ebullioscopic in acetone), 368. $C_{21}H_{18}O_9$ requires C, 60·9; H, 4·3%; *M*, 414], $\lambda_{max.}$ 365 and 231 mμ (log ε 4·38 and 4·26), dissolving slowly in 2N-sodium hydroxide to a red solution.

3-*Acetylhispidin.*—3-Acetylhispidin triacetate (0·25 g.) was refluxed with ethanol (20 ml.) and 2N-sulphuric acid (20 ml.) for 45 min.; this gave orange-red plates of 3-*acetylhispidin* (0·16 g.), m. p. 306° (decomp.) (from acetic acid) (Found: C, 62·7; H, 4·2. $C_{15}H_{12}O_6$ requires

C, 62·5; H, 4·2%), $\lambda_{max.}$ 410 and 260 mμ (log ε 4·40 and 3·99). This afforded a *2,4-dinitrophenylhydrazone*, red rhombs (from dioxan), m. p. 279° (Found: N, 12·0. $C_{21}H_{16}N_4O_9$ requires N, 12·0%).

3-Acetylhispidin Trimethyl Ether.—3-Acetylhispidin (0·9 g.), acetone (45 ml.), potassium carbonate (18 g.), and dimethyl sulphate (9 ml.) were refluxed for 6 hr., cooled, filtered, and evaporated under a vacuum. The orange residue, recrystallised three times from alcohol, gave the *trimethyl ether* as golden-yellow needles (0·27 g.), m. p. 182° (Found: C, 65·4; H, 5·4. $C_{18}H_{18}O_8$ requires C, 65·4; H, 5·4%), $\lambda_{max.}$ 404 and 255 mμ (log ε 4·44 and 4·17). This gave a *2,4-dinitrophenylhydrazone*, red needles (from acetic acid), m. p. 209° (Found: N, 11·2. $C_{24}H_{22}N_4O_9$ requires N, 11·0%).

3-Acetylhispidin Dimethyl Ether.—3-Acetylhispidin (5 g.), acetone (25 ml.), methyl iodide (7·0 g.), and potassium carbonate (4·0 g.) were refluxed for 18 hr., then evaporated. Water (25 ml.) was added and the mixture was cooled in ice and shaken. The red oil, which rapidly solidified, was filtered off and recrystallised from alcohol (2·5 ml.) to yield the trimethyl ether (0·17 g.). The mother-liquor was acidified with dilute hydrochloric acid, and the precipitate recrystallised three times from acetic acid to give the *dimethyl ether* as orange-yellow needles (0·2 g.), m. p. 213° (Found: C, 64·5; H, 5·1. $C_{17}H_{16}O_8$ requires C, 64·4; H, 5·1%), $\lambda_{max.}$ 399 and 258i mμ (log ε 4·36 and 4·02). The latter gave a *2,4-dinitrophenylhydrazone*, orange-red needles (from acetic acid), m. p. 299° (Found: N, 11·6. $C_{23}H_{20}N_4O_9$ requires N, 11·3%).

3-Acetylhispidin Dibenzoate.—Benzoylation of 3-acetylhispidin in pyridine at room temperature gave yellow needles of the *dibenzoate*, m. p. 186° (from acetic acid) (Found: C, 70·1; H, 4·0. $C_{29}H_{20}O_8$ requires C, 70·2; H, 4·0%), dissolving slowly in cold sodium hydroxide to a yellow solution. This product was not formed if the reaction mixture was heated.

3-Acetyldihydrohispidin Diacetate.—3-Acetylhispidin triacetate (2·0 g.) in ethyl acetate (100 ml.) was shaken with hydrogen at atmospheric pressure in the presence of Adams catalyst (0·1 g.) (absorption 180 ml.) for 12 hr. The solution was filtered and evaporated *in vacuo*. The residual oil was extracted with hot light petroleum (150 ml.; b. p. 80—100°). Colourless plates of *3-acetyldihydrohispidin diacetate* (0·6 g.) were deposited on cooling and after recrystallising twice from alcohol and once from light petroleum had m. p. 121° (Found: C, 60·9; H, 4·9. $C_{18}H_{18}O_8$ requires C, 60·9; H, 4·9%), $\lambda_{max.}$ 311 mμ (log ε 4·10).

Similarly 3-acetylhispidin dimethyl ether (0·5 g.) yielded *3-acetyldihydrohispidin dimethyl ether* (0·34 g.) as pale yellow plates, m. p. 141° (from alcohol) (Found: C, 64·1; H, 5·7. $C_{17}H_{18}O_8$ requires C, 64·1; H, 5·7%), $\lambda_{max.}$ 308 mμ (log ε 3·98).

3-Acetyldihydrohispidin.—3-Acetyldihydrohispidin diacetate (0·4 g.), on acid hydrolysis, gave yellow needles of *3-acetyldihydrohispidin* (0·28 g.) which, after crystallising from dilute alcohol and then from toluene, formed yellow needles, m. p. 188° (Found: C, 61·9; H, 4·8. $C_{15}H_{14}O_8$ requires C, 62·1; H, 4·9%), $\lambda_{max.}$ 312 mμ (log ε 4·09) [*2,4-dinitrophenylhydrazone*, orange red plates (from acetic acid), m. p. 241° (Found: N, 11·7. $C_{21}H_{18}N_4O_9$ requires N, 11·9%)].

Di-O-acetyldihydrohispidin.—Di-*O*-acetylhispidin (0·5 g.) was hydrogenated at atmospheric pressure over 5% palladium–charcoal (0·15 g.). The reaction was stopped after absorption of 1·2 mol. of hydrogen (45 min.). Filtration and evaporation, followed by recrystallisation from toluene, gave colourless plates (0·2 g.) of *di-O-acetyldihydrohispidin*, m. p. 155° (Found: C, 61·6; H, 5·1. $C_{17}H_{16}O_7$ requires C, 61·4; H, 4·8), $\lambda_{max.}$ 285 mμ (log ε 3·92). An alcohol solution of this product gives a characteristic purple-brown colour, which changes to red and then becomes colourless on addition of sodium hydroxide solution.

Acid hydrolysis of this diacetate gave needles of *dihydrohispidin monohydrate*, m. p. 104—108° (from hot water) (Found: C, 58·5; H, 5·6. $C_{13}H_{12}O_5,H_2O$ requires C, 58·6; H, 5·3%), $\lambda_{max.}$ 285 mμ (log ε 3·97).

6-(3,4-Dimethoxyphenyl)hex-5-ene-2,4-dione (III).—Tri-*O*-methylhispidin (0·5 g.) in N-ethanolic potassium hydroxide (200 ml.) was set aside at room temperature in a stream of nitrogen for 36 hr. Yellow plates of the potassium salt of the acid (II) slowly separated. These (0·57 g.) were collected, washed with absolute alcohol, and dried in air. Cautious acidification of an aqueous solution of this salt gave the free acid as an amorphous yellow solid. The potassium salt (0·2 g.) was refluxed for 1 hr. with 2N-sulphuric acid (5 ml.) and ethanol (3 ml.) Pale yellow plates of the *diketone* (0·04 g.) were deposited on cooling; recrystallised from light petroleum they had m. p. 92° (Found: C, 67·5; H, 6·5. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·45%).

Di-O-methylhispidin.—The acid (II) (0·3 g.) was refluxed with acetic anhydride (5 ml.) for

1 hr., then poured into water (50 ml.). The resulting yellow oil slowly solidified, to yield di-*O*-methylhispidin, m. p. 184° (decomp.) (from alcohol) (Found: C, 61·6; H, 5·8%), $\lambda_{max.}$ 366, 251i mμ (log ε 4·15, 4·07). Tri-*O*-methylhispidin, identified by its infrared spectrum and mixed m. p., was obtained from this compound by treatment with diazomethane.

Oxidation of 3-*Acetylhispidin Triacetate.*—This compound (1·2 g.), dissolved in acetic acid (36 ml.) and acetic anhydride (36 ml.), was heated at 55—60° with stirring while chromium trioxide (2·4 g.) in water (1·8 ml.) and glacial acetic acid (25 ml.) was added. The temperature was kept at 65—70° for 4 hr., then the solution was poured into water (500 ml.). After filtration the filtrate was extracted with ether for 3 hr.; the extract was evaporated to 180 ml. and washed with saturated sodium hydrogen carbonate solution (1 × 200 ml., 2 × 100 ml.). The sodium hydrogen carbonate extract was acidified with 30% hydrochloric acid and extracted with ether (2 × 200 ml., 2 × 100 ml.). The ethereal solution was washed, dried, and evaporated, to yield a waxy yellow residue which, after recrystallisation from benzene, provided 0·2 g. of colourless needles, m. p. 146—148°. Repeated recrystallisation from water raised the m. p. to 157°. The product was identical with protocatechuic acid diacetate (m. p., mixed m. p., and infrared spectrum) (Found: C, 55·4; H, 4·3. Calc. for $C_{11}H_{10}O_6$: C, 55·5; H, 4·2%).

Oxidation of di-*O*-acetylhispidin yielded the same acetate, m. p. 157°.

*Ozonolysis of Tri-*O*-acetylhispidin.*—Ozonised oxygen was passed for 20 min. through a solution of tri-*O*-acetylhispidin (0·66 g.) in chloroform (15 ml.) cooled in isopropyl alcohol and solid carbon dioxide. Shaking the mixture with water (30 ml.) for 2·5 hr., followed by separation of the organic layer, drying, and removal of the solvent gave a residue. The 2,5-dinitrophenylhydrazone of this residue was purified by chromatography on acid-washed alumina from chloroform, and identified as the 2,4-dinitrophenylhydrazone (18 mg.) of protocatechualdehyde diacetate by m. p. and mixed m. p. (212°) (Found: C, 51·1; H, 3·5; N, 13·9. Calc. for $C_{17}H_{14}N_4O_8$: C, 50·75; H, 3·5; N, 13·9%).

Oxidation of 3-*Acetylhispidin Trimethyl Ether.*—A refluxing acetone solution of this ether (0·5 g. in 30 ml.) was treated portion-wise with solid potassium permanganate until a faint permanent pink colour developed. The solvent was removed, water was added, and sulphur dioxide passed into the solution until all the manganese dioxide had dissolved. The solution was steam-distilled and the distillate (200 ml.) acidified and extracted with ether. Evaporation of the dried extract yielded only 5 mg. of an oil which was not identified. The residual aqueous solution was acidified and extracted with ether (3 × 20 ml.); evaporation of the dried ether extract yielded veratric acid (80 mg.) which, after sublimation *in vacuo* and recrystallisation from light petroleum ether, had m. p. and mixed m. p. 181° (Found: C, 59·6; H, 5·7. Calc. for $C_9H_{10}O_4$: C, 59·3; H, 5·9%).

*Synthesis of Tri-*O*-methylhispidin.*—Veratraldehyde (5·0 g.) and 4-methoxy-6-methyl-2-pyrone (4·2 g.) (from triacetic lactone and dimethyl sulphate) were refluxed for 4 hr. with magnesium methoxide (from 2·0 g. of magnesium and 100 ml. of methanol). After 4 hr., more methanol (100 ml.) was added and the solution filtered. The deposited yellow tri-*O*-methylhispidin (1·2 g.) was filtered off and the filtrate evaporated to dryness. The gummy residue was treated with 2N-sulphuric acid (10 ml.), and the residue dissolved in chloroform, which, after being washed with water and dried (Na_2SO_4), was chromatographed on magnesium oxide (B.D.H. chromatographic grade). The eluted yellow band yielded an oil which on trituration with methanol yielded *tri-*O*-methylhispidin* (0·75 g.) as yellow needles, m. p. and mixed m. p. 164° (Found: C, 66·6; H, 5·5; OMe, 29·3. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6; OMe, 32·3%), $\lambda_{max.}$ 366 and 251 mμ (log ε 4·39 and 4·17) (cf. Fig. 1).

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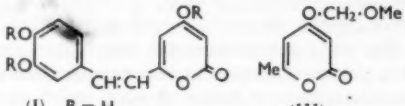
984. *Constituents of the Higher Fungi. Part II.*[1] *The Synthesis of Hispidin.*

By R. L. Edwards and D. V. Wilson.

Hispidin has been synthesised by two methods. Methoxymethyl groups have been used to protect the phenolic hydroxyl groups of the starting materials.

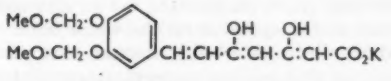
In Part I [1] the isolation and elucidation of the structure of a new 4-hydroxy-6-styryl-2-pyrone (I) from the basidiomycete *Polyporus hispidus* (Bull.) Fr. was described. We now report its synthesis.

6-Styryl-2-pyrones have been synthesised by condensing an acid chloride with acetonedicarboxylic acid and cyclising the product,[2] and by condensing an aromatic aldehyde with 4-methoxy-6-methyl-2-pyrone in the presence of magnesium methoxide.[1,3] The latter method failed to yield a condensation product from protocatechualdehyde, doubtless because the phenolic hydroxyl groups prevent aldol condensation.[4] In the protection of hydroxyl groups, methoxymethyl ethers are readily cleaved by acids [5] and they have been



(I) R = H
(II) R = MeO·CH$_2$

(III)



(IV)

used for the preparation of hydroxycinnamaldehydes.[6] 4-Hydroxy-6-methyl-2-pyrone readily formed the 4-methoxymethyl ether (III) on reaction with chloromethyl ether in the presence of anhydrous potassium carbonate, the identity of the product being established from its ultraviolet spectrum; the 2-methoxymethyl ether was not detected. Protocatechualdehyde dimethoxymethyl ether was prepared in 50% yield from chloromethyl ether and the sodium salt of the aldehyde suspended in dry toluene: condensation of these two protected compounds in the presence of magnesium methoxide gave only a low yield of the required 6-[3,4-di(methoxymethoxy)styryl]-4-methoxymethoxy-2-pyrone (II) which was difficult to separate from the accompanying yellow oil but hydrolysis with boiling 2N-acid gave hispidin in quantitative yield.

An alternative procedure giving a much higher overall yield involved condensation of protocatechualdehyde dimethoxymethyl ether with the 4-methyl instead of the methoxymethyl ether. The styrylpyrone, obtained in good yield, was hydrolysed to the potassium salt (IV) by ethanolic potassium hydroxide; the free acid gave tri-*O*-acetylhispidin in refluxing acetic anhydride and thence hispidin on acid hydrolysis.

Experimental

4-Methoxymethoxy-6-methyl-2-pyrone.—Chloromethyl ether [7] (16 ml.) was added during 15 min. to a stirred, refluxing solution of 4-hydroxy-6-methyl-2-pyrone (triacetic lactone) [8] (10 g.) in dry acetone (200 ml.) containing anhydrous potassium carbonate (30 g.). The

[1] Part I, Edwards, Lewis, and Wilson, preceding paper.
[2] Borsche and Bodenstein, *Ber.*, 1929, **62**, 2513; Zdzistaw and Macierewiez, *Roczniki Chem.*, 1950, **24**, 144.
[3] Bu'Lock and Smith, *J.*, 1960, 502.
[4] Tiemann, *Ber.*, 1885, **18**, 3482.
[5] Hoering and Baum, G.P. 209,608.
[6] Pauly and Wascher, *Ber.*, 1923, **56**, 603; Pauly and Strassberger, *Ber.*, 1929, **62**, 2277.
[7] *Org. Synth.*, 1929, **9**, 58.
[8] Collie, *J.*, 1891, **59**, 607.

mixture was allowed to cool and filtered, the solid being washed with acetone. Evaporation gave an oil which was washed in ether (30 ml.) with 2N-sodium hydroxide, then with water (30 ml.), dried (Na_2SO_4), and evaporated. The residue was repeatedly extracted with hot light petroleum (b. p. 40—60°), which afforded needles of *4-methoxymethoxy-6-methyl-2-pyrone* (6·3 g.), m. p. 57° (from light petroleum) (Found: C, 56·5; H, 6·2. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%), $\lambda_{max.}$ 280 mμ.

3,4-Di(methoxymethoxy)benzaldehyde.—To protocatechualdehyde (69 g.) in stirred boiling toluene (600 ml.), sodium ethoxide [from sodium (23 g.) and absolute alcohol (300 ml.)] was added during 30 min., alcohol being meanwhile removed in a stream of nitrogen. The remaining alcohol was distilled off and the residue was cooled to 0° and treated with chloromethyl ether (81 g.) during 3 hr., stirred at room temperature for 4 hr., and shaken with 2N-sodium hydroxide (100 ml.). The toluene layer was separated, washed with water, dried (Na_2SO_4), and evaporated. The residue brown oil was distilled at 3 mm.; the fraction boiling up to 160° was collected: it solidified. A small quantity of contaminant insoluble in acid and alkali was removed by dissolving the distilled product in alcohol (60 ml.) and adding water until an oil separated. The colourless suspended solid was filtered off and the filtrate vigorously shaken; the oil rapidly solidified to yield *3,4-di(methoxymethoxy)benzaldehyde*, which after recrystallising twice from light petroleum (b. p. 80—100°) formed needles, m. p. 60° (Found: C, 58·1; H, 6·2. $C_{11}H_{14}O_5$ requires C, 58·4; H, 6·15%).

6-[3,4-Di(methoxymethoxy)styryl]-4-methoxymethoxy-2-pyrone.—3,4-Di(methoxymethoxy)-benzaldehyde (1·07 g.), 6-methyl-4-methoxymethoxy-2-pyrone (0·85 g.), and magnesium methoxide (from magnesium, 0·4 g., and methyl alcohol, 20 ml.) were refluxed for 4 hr., then filtered and evaporated on the water bath. The residue was extracted with light petroleum (100 ml.; b. p. 80—100°); cooling this gave a yellow oil which at low temperature slowly deposited *6-[3,4-di(methoxymethoxy)styryl]-4-methoxymethoxy-2-pyrone* (3 mg.), which recrystallised from light petroleum–ether as pale yellow cubes, m. p. 59—60° (Found: C, 60·1; H, 5·9. $C_{19}H_{22}O_8$ requires C, 60·3; H, 5·8%).

6-(3,4-Dihydroxystyryl)-4-hydroxy-2-pyrone (*Hispidin*).—The foregoing ether (30 mg.) was boiled in water (10 ml.) containing 2N-sulphuric acid (3 drops) for 3 min. On cooling, hispidin was precipitated (19 mg.), with m. p. and mixed m. p. 259° (decomp.) (correct ultraviolet and infrared spectrum).

6-[3,4-Di(methoxymethoxy)styryl]-4-methoxy-2-pyrone.—3,4-Di(methoxymethoxy)benzaldehyde (2·15 g.) and 4-methoxy-6-methyl-2-pyrone were condensed as described above. The methanol solution was evaporated and the residue washed in chloroform with 2N-sulphuric acid (20 ml.) and water, dried (Na_2SO_4), and placed on magnesium oxide; evaporation of the eluate gave the solid *pyrone* (0·76 g.), pale yellow needles, softening at 107°, m. p. 116° (from methanol) (Found: C, 61·9; H, 5·8. $C_{19}H_{20}O_7$ requires C, 62·1; H, 5·75%).

This ether (0·5 g.) was hydrolysed by boiling 2N-sulphuric acid in 5 min. to *O*-methylhispidin, orange-yellow needles, m. p. and mixed m. p. 257° (decomp) (from glacial acetic acid) (Found: C, 64·5; H, 4·9. Calculated for $C_{14}H_{12}O_5$: C, 64·6; H, 4·6%).

The triether (0·65 g.) in ethanol (50 ml.) at 5° was treated with potassium hydroxide (8 g.) in ethanol (180 ml.). The mixture was set aside at room temperature in a stream of nitrogen for 48 hr. The precipitated potassium *7-[3,4-di(methoxymethoxy)phenyl]-3,5-dihydroxy-hepta-2,4,6-trienoate* (0·4 g.) was separated, washed with absolute alcohol, and dissolved in water (10 ml.). Acidification of the solution with dilute sulphuric acid yielded the free acid with spontaneous removal of the methoxymethyl groups. The yellow acid was air-dried and refluxed with acetic anhydride (3 ml.) for 3 min.; pouring the mixture into water gave orange-yellow tri-*O*-acetylhispidin (135 mg.) which after recrystallisation twice from alcohol had m. p. 143° (Found: C, 61·3; H, 4·4. Calc. for $C_{19}H_{16}O_8$: C, 61·3; H, 4·3%). Hydrolysis of this acetate as described in Part I [1] yielded hispidin, m. p. and mixed m. p. 259° (decomp.).

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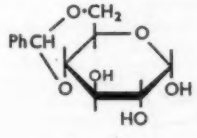
985. *Aspects of Stereochemistry. Part VIII.* Determination of the Configuration at the Benzylidene Acetal Carbon Atoms in* 4,6-O-*Benzylidene-*D-*glucose and* 1,3-O-*Benzylidene-*L-*arabinitol by Nuclear Magnetic Resonance Spectroscopy.*

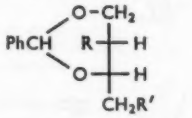
By A. B. Foster, A. H. Haines, J. Homer, J. Lehmann, and L. F. Thomas.

4,6-*O*-Benzylidene-D-glucose and 1,3-*O*-benzylidene-L-arabinitol have been degraded to 1,3-*O*-benzylidene-L-erythritol and 1,3-*O*-benzylidene-L-threitol, respectively. It has been shown that the latter two compounds differ only in the configuration at $C_{(2)}$. From the nuclear magnetic resonance spectra of the acetates of the tetritol derivatives and of related compounds the configuration of the phenyl group relative to the other substituents of the 1,3-dioxan rings has been deduced.

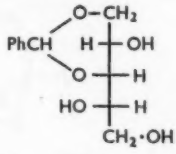
In the reaction of aldehydes, other than formaldehyde, with polyhydric alcohols to yield cyclic acetals, the formation of diastereoisomers is theoretically possible. Since the acid-catalysed reaction which yields cyclic acetals is reversible,[1] the products formed should be those of greatest thermodynamic stability. When five-membered cyclic acetals (1,3-dioxolan derivatives) are produced there is no reason to expect *a priori* the preferential formation of one diastereoisomer and various pairs of diastereoisomers are known.[2] A different situation exists when six-membered cyclic acetals (1,3-dioxan derivatives) are formed. If, as is probable, the 1,3-dioxan ring assumes a chair conformation,[1] then the diastereoisomers will have respectively an equatorial and an axial substituent at the acetal carbon atom. Because of adverse non-bonded interactions, the latter configuration will be relatively unstable and it has been predicted[3] that such a diastereoisomer is unlikely to be formed. Certain benzylidene derivatives described in the literature,[4] which were



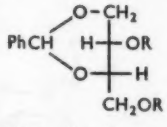
(I)



(II) R = R′ = OH
(III) R = OH, R′ = H
(IV) R = R′ = AcO
(V) R = R′ = BzO



(VI)



(VII) R = H
(VIII) R = Ac
(IX) R = Me·SO2

considered to be examples of diastereoisomers, have been shown to be dimorphs.[2] There is no substantiated example of the formation of diastereoisomers in the reaction of benzaldehyde with tetritols and higher polyhydric alcohols to yield six-membered cyclic acetals. Moreover, in no case has experimental evidence been recorded which would indicate the configuration of the benzylidene acetal carbon atoms. The 5-hydroxy-2-phenyl-1,3-dioxans[5] (1,3-*O*-benzylideneglycerols) and their *p*-nitrophenyl analogues[6] are anomalous in that they may be considered as diastereoisomeric at $C_{(2)}$ or $C_{(5)}$. We now record direct experimental evidence of the configuration at the benzylidene acetal carbon atoms in 4,6-*O*-benzylidene-D-glucose and 1,3-*O*-benzylidene-L-arabinitol.

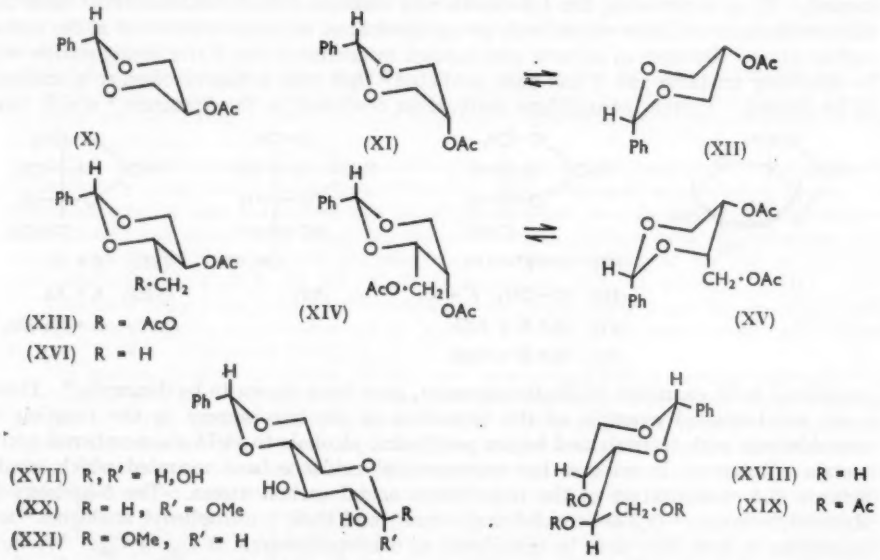
* Part VII, *J.*, 1961, 3633.

[1] Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.
[2] Dobinson, Foster, and Stacey, *Tetrahedron Letters*, 1959, No. 1, p. 1.
[3] Angyal and Mills, *Rev. Pure Appl. Chem.* (*Australia*), 1952, **2**, 185.
[4] Fischer, *Annalen*, 1892, **270**, 64; *Ber.*, 1894, **27**, 1524; Hann, Ness, and Hudson, *J. Amer. Chem. Soc.*, 1946, **68**, 1769; Ness, Hann, and Hudson, *ibid.*, 1948, **70**, 765.
[5] Baggett, Brimacombe, Foster, Stacey, and Whiffen, *J.*, 1960, 2574.
[6] Dobinson and Foster, *J.*, 1961, 2338.

4,6-*O*-Benzylidene-D-glucose (I), the structure of which other than at the acetal carbon atom has been proved,[7] was oxidised with sodium metaperiodate and the resultant 2,4-*O*-benzylidene-D-erythrose [8] was smoothly reduced with sodium borohydride to 1,3-*O*-benzylidene-L-erythritol (II). The diol (II) gave a crystalline di-*O*-acetate, di-*O*-benzoate, and di-*O*-toluene-*p*-sulphonate; the di-*O*-methanesulphonate was amorphous. Reduction of the di-*O*-toluene-*p*-sulphonate with lithium aluminium hydride afforded 1,3-*O*-benzylidene-4-deoxy-L-erythritol (III).

In the presence of acid, D-arabinitol reacts [9] with benzaldehyde to yield a 1,3-*O*-benzylidene derivative (m. p. 151—152°, $[\alpha]_D$ −7·6° in pyridine), for which the location of the cyclic acetal residue has been fully proved.[9] We have used the corresponding derivative (VI) (m. p. 149—151°, $[\alpha]_D$ +7·2° in pyridine) of L-arabinitol the structure of which is confirmed by the physical constants. Application, in sequence, of periodate oxidation and borohydride reduction to 1,3-*O*-benzylidene-L-arabinitol, afforded 1,3-*O*-benzylidene-L-threitol (VII) which gave a crystalline di-*O*-toluene-*p*-sulphonate, di-*O*-methanesulphonate, and di-*O*-acetate. Reduction of the dimethanesulphonate with lithium aluminium hydride yielded 1,3-*O*-benzylidene-L-threitol as the only identifiable product. Under similar conditions the analogous di-*O*-toluene-*p*-sulphonate afforded only a small yield of a product tentatively identified as 1,3-*O*-benzylidene-4-deoxy-L-threitol which was isolated by way of the *p*-phenylazobenzoate.

The structural relationship of 1,3-*O*-benzylidene-L-threitol (VII) and 1,3-*O*-benzylidene-L-erythritol (II) was shown by the conversion of the di-*O*-methanesulphonate (IX) of the former compound into the di-*O*-benzoate (V) of the latter by treatment with sodium



benzoate in dimethylformamide. The nucleophilic displacement of a sulphonyloxy-group by this reagent was first described by Reist *et al.*,[10] who converted methyl 2,3-di-*O*-benzoyl-4,6-di-*O*-toluene-*p*-sulphonyl-α-D-galactopyranoside into methyl 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranoside. Methanesulphonyloxy-groups are displaced with equal

[7] Freudenberg, Toepffer, and Andersen, *Ber.*, 1928, **61**, 1750.
[8] MacDonald, Fischer, and Ballou, *J. Amer. Chem. Soc.*, 1956, **78**, 3720; Sowden, *ibid.*, 1950, **72**, 808.
[9] Haskins, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 1663.
[10] Reist, Spencer, and Baker, *J. Org. Chem.*, 1959, **24**, 1618.

facility: for example, *cis*- and *trans*-5-methanesulphonyloxy-2-phenyl-1,3-dioxan are converted, respectively, into *trans*- and *cis*-5-benzoyloxy-2-phenyl-1,3-dioxan.[11] Thus 1,3-*O*-benzylidene-L-threitol and 1,3-*O*-benzylidene-L-erythritol differ only in the configuration at $C_{(2)}$. The location of the cyclic acetal residue and the stereochemistry of the tetritol moiety ensure that the 2-hydroxyl group and the hydroxymethyl group in 1,3-*O*-benzylidene-L-erythritol are *trans*-substituents in the 1,3-dioxan ring and likewise the corresponding groups in 1,3-*O*-benzylidene-L-threitol are *cis*-disposed. The configuration of the phenyl group at the acetal carbon atom relative to the other substituents of the 1,3-dioxan rings in these compounds may be deduced from the proton magnetic resonance spectra of their acetates and of related compounds, the relevant signals for which are recorded in the Table. A full analysis of the spectra of these compounds is reserved for a separate communication. A preliminary report has been made.[12]

It has been found[12] that *trans*-5-acetoxy-2-phenyl-1,3-dioxan (1,3-*O*-benzylideneglycerol) gave a type *X* * proton magnetic resonance spectrum showing a complex coupling pattern for the ring protons indicative of molecular rigidity and existence in conformation (X). The ring substituents may therefore be assigned to definite equatorial or axial positions. The *cis*-isomer, however, gave a simpler, type *Y* * spectrum which contained a single broad absorption for the protons at positions 4 and 6, indicating conformational instability and a relatively rapid interconversion between different conformations. The ring substituents therefore cannot be assigned to specific axial or equatorial positions but must occupy an average or intermediate position. The interconversion has, for convenience, been represented by the formulæ (XI) $\rightleftharpoons$ (XII) although it is recognised that the extreme positions in the interconversion may not necessarily involve the perfect

Selected shielding values from the nuclear magnetic resonance spectra of certain 1,3-dioxan derivatives.

Compound	Spectrum type	Conformn.	Shielding value [a] A	B	C
trans-5-Acetoxy-2-phenyl-1,3-dioxan	*X*	(X)	4·61	8·00	
2,4-Di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol	*X*	(XIII)	4·54	7·97	7·97
2-*O*-Acetyl-1,3-*O*-benzylidene-4-deoxy-L-erythritol	*X*	(XVI)	4·56	7·99	
Me 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside	*X*	(XX)	4·54		7·97 (2)
Me 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside	*X*	(XXI)	4·54		7·97 (2)
cis-5-Acetoxy-2-phenyl-1,3-dioxan	*Y*	(XI) $\rightleftharpoons$ (XII)	4·51	7·88	
2,4-Di-*O*-acetyl-1,3-*O*-benzylidene-L-threitol	*Y*	(XIV) $\rightleftharpoons$ (XV)	4·47	7·90	7·99
2,4,5-Tri-*O*-acetyl-1,3-*O*-benzylidene-L-arabinitol	*Y*	(XIX) [b]	4·45	7·91	7·98 (2)

[a] A, proton at benzylidene acetal carbon atom; B, acetyl protons in $CH_3{\cdot}CO{\cdot}O$ groups attached to dioxan ring; C, protons in side chain and other acetyl group(s). Relative intensity in parentheses if other than unity. [b] Only one conformation is shown although the molecule is conformationally unstable.

chair forms shown. Non-bonded interactions may cause deformation of the perfect chair forms but the extent is difficult to assess. For *trans*-5-acetoxy-2-phenyl-1,3-dioxan (X) the shielding value (τ 4·61) for the axial proton on the acetal carbon atom was higher than that (τ 4·51) for the corresponding proton in the *cis*-isomer (XI) $\rightleftharpoons$ (XII), which is intermediate between axial and equatorial. Further, the equatorial acetyl group in the *trans*-isomer (X) had a higher shielding value (τ 8·00) for the protons than that (τ 7·88) for the protons of the acetyl group in the *cis*-isomer which again must be intermediate between

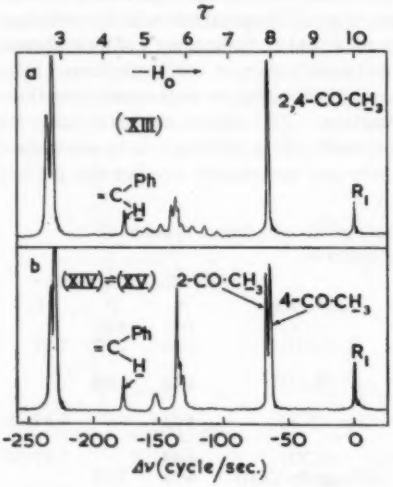
* The terms type *X* and *Y* have been introduced[13] solely for convenience of discussion. It is not intended that they should be of general application.

[11] Bukhari, Foster, and Lehmann, unpublished results.
[12] Baggett, Dobinson, Foster, Homer, and Thomas, *Chem. and Ind.*, 1961, 106.

XUM

axial and equatorial. These observations are consistent with those recorded by Lemieux *et al.*[13] for certain acetylated pyranose sugar derivatives.

2,4-Di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol (IV) gave a type *X* spectrum (see Figure) with a complex coupling pattern (τ 5—7) indicative of molecular rigidity, whereas the L-threitol isomer (VIII) gave a type *Y* spectrum (see Figure) suggestive of conformational instability. By analogy with the results for the 5-acetoxy-2-phenyl-1,3-dioxans, the proton on the benzylidene acetal carbon atom in 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol (IV) may be assigned an axial position since its shielding value (τ 4·54) is higher than that (τ 4·47) for the corresponding proton in the conformationally unstable L-threitol analogue (VIII). Hence, the phenyl group in the L-erythritol derivative (IV) must be equatorial. Further, the L-erythritol compound (IV) gave a single peak (τ 7·97) for both the groups of acetyl protons. That the acetoxy-group in this derivative (IV) (and hence the acetoxymethyl group also) is equatorial to the 1,3-dioxan ring is suggested by the similarity of the shielding value (τ 7·97) for its protons to that (τ 8·00) for the acetyl protons in *trans*-5-acetoxy-2-phenyl-1,3-dioxan (X) which has the



Nuclear magnetic resonance spectra of (a) 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol (type X) and (b) 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-threitol (type Y).

acetoxyl group equatorial. 2,4-Di-*O*-acetyl-1,3-*O*-benzylidene-L-threitol (VIII) gave two peaks (τ 7·90 and 7·99) for the two groups of acetyl protons. The absorption at τ 7·90 corresponds well with that (τ 7·88) for the acetyl protons in *cis*-5-acetoxy-2-phenyl-1,3-dioxan (XI) ⇌ (XII) and hence may be assigned to the protons in the 2-acetyl group in the conformationally unstable L-threitol derivative (VIII). Since the shielding value (τ 7·97) for the 2-acetyl protons in 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol (IV) is higher than that (τ 7·90) for the protons in the corresponding acetyl group in the L-threitol analogue (VIII) the equatorial location of the former acetyl group is substantiated. The shielding values (τ 7·99, 7·97 respectively) for the acetyl protons in the acetoxymethyl groups in 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol (IV) and the L-threitol analogue (VIII) are similar. Since the former cyclic acetal is a rigid molecule and the latter is conformationally unstable the signal for the acetyl protons in the acetoxymethyl group appears to be independent of the conformation of the 1,3-dioxan ring.

It follows that if the 2-acetoxy-group in 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol is equatorial, then the acetoxymethyl group is also equatorial and since the phenyl group is similarly located the structure of the cyclic acetal is completely defined by formula

[13] Lemieux, Kullnig, Bernstein, and Schneider, *J. Amer. Chem. Soc.*, 1958, **80**, 6098.

(XIII). Further, since it has been shown that 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol (IV) and its L-threitol analogue differ only in the configuration at $C_{(2)}$, the latter compound must have the structure represented by the equilibrium (XIV) $\rightleftharpoons$ (XV).

Replacement of the acetoxymethyl group in the L-erythritol compound (XIII) by methyl to give 2-*O*-acetyl-1,3-*O*-benzylidene-4-deoxy-L-erythritol (XVI) does not affect significantly the shielding values for the proton on the benzylidene acetal carbon atom and for the 2-acetyl protons.

Since 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol has the structure (XIII), the configuration of the parent compound, 4,6-*O*-benzylidene-D-glucose, may be defined as in formula (XVII) which contains a *trans*-decalin type ring system with the phenyl group equatorial to the 1,3-dioxan ring. This is the predicted [3] structure. It is noteworthy that 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol and methyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α- and -β-D-glucopyranoside exhibit the same shielding value (τ 4·54) for the protons at the benzylidene acetal carbon atoms and for the acetyl protons (τ 7·97). The structures (XX) and (XXI) may therefore be allocated to the glucosides.

2,4,5-Tri-*O*-acetyl-1,3-*O*-benzylidene-L-arabinitol (XIX) also gave a type *Y* spectrum indicative of conformational instability. There is a close correspondence (see Table) between the shielding values for the protons on the benzylidene acetal carbon atoms and for the various groups of acetyl protons in the L-arabinitol derivative (XIX) and in 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-threitol (XIV) $\rightleftharpoons$ (XV). The shielding value at τ 7·98 for the former compound was twice the intensity of that at τ 7·99 in the latter since it arises from both the side-chain acetyl groups. The larger side chain in the former compound than in the latter is not sufficient to confer molecular rigidity. Although 2,4,5-tri-*O*-acetyl-1,3-*O*-benzylidene-L-arabinitol is conformationally unstable it is possible that this is not the case for the parent compound 1,3-*O*-benzylidene-L-arabinitol. The reaction of L-arabinitol with benzaldehyde to yield a 1,3- but not a 3,5-*O*-benzylidene derivative has been attributed [5,14] to an intramolecular hydrogen-bonding effect which would be operative only in the conformation (XVIII).

Experimental

1,3-O-*Benzylidene-L-erythritol*.—4,6-*O*-Benzylidene-D-glucose [7] (40 g.) was oxidised with periodate, and the product reduced with sodium borohydride by essentially the method of MacDonald *et al.*[8] After destruction of the excess of borohydride with acetic acid, the neutral solution was added to a column (3 × 20 cm.) of Ultrasorb,[15] and inorganic material was eluted with water. Subsequent elution with aqueous alcohol (1 : 4 v/v), concentration of the eluate, and recrystallisation of the residue from benzene–light petroleum (b. p. 60—80°) gave 1,3-*O*-benzylidene-L-erythritol (22·5 g., 75%), m. p. 135—137° $[\alpha]_D$ −14° (*c* 0·5 in $CHCl_3$), $[M]$ −29°, $[\alpha]_D$ −41° (*c* 0·8 in MeOH), $[M]_D$ −86°. MacDonald *et al.*[8] record m. p. 135—136°, $[\alpha]_D$ −43° in MeOH.

Sulphonylation of the product in the usual way gave 1,3-O-*benzylidene*-2,4-*di*-O-*toluene*-p-*sulphonyl*-L-*erythritol*, m. p. 184° (decomp.) (from benzene–chloroform), $[\alpha]_D$ −49° (*c* 1·0 in $CHCl_3$), $[M]_D$ −210° (Found: C, 57·7; H, 5·0; S, 12·4. $C_{32}H_{36}O_8S_2$ requires C, 57·9; H, 5·05; S, 12·4%). The *di*-O-*methanesulphonate* was amorphous (Found: C, 42·6; H, 4·9; S, 18·0. $C_{18}H_{18}O_8S_2$ requires C, 42·6; H, 5·0; S, 17·5%).

Likewise acylation in the usual manner gave 2,4-di-*O*-acetyl-1,3-*O*-benzylidene-L-erythritol,[16] m. p. 81—83·5°, $[\alpha]_D$ −40° (*c* 0·27 in $CHCl_3$), $[M]_D$ −118°, and 2,4-*di*-O-*benzoyl*-1,3-O-*benzylidene*-L-*erythritol* (33%), m. p. 84—85°, $[\alpha]_{5461}$ −89° (*c* 0·5 in $CHCl_3$), $[M]_{5461}$ −372° (Found: C, 71·75; H, 5·3. $C_{32}H_{28}O_6$ requires C, 71·7; H, 5·3%).

1,3-O-*Benzylidene*-4-*deoxy*-L-*erythritol*.—A suspension of 1,3-*O*-benzylidene-2,4-di-*O*-toluene-*p*-sulphonyl-L-erythritol (24 g.) in tetrahydrofuran (150 ml.) was treated slowly with a slurry of lithium aluminium hydride (9 g.) in tetrahydrofuran (50 ml.), and the mixture was boiled under reflux for 10 hr. A further amount (2 g.) of reductant was added and heating

[14] Brimacombe, Foster, and Stacey, *Chem. and Ind.*, 1958, 1228.
[15] Hughes and Whelan, *Chem. and Ind.*, 1958, 884.
[16] Foster, Haines, and Lehmann, *J.*, 1961, 5011.

was continued for a further 50 hr. The cooled mixture was diluted with ether (200 ml.), the excess of reductant was decomposed with ethyl acetate, and subsequently the alcoholates by addition of water (15—20 ml.). Insoluble inorganic material was collected and washed with ether, and the combined and dried (Na_2SO_4) filtrate and washings were concentrated. The oily residue crystallised from ether–light petroleum (b. p. 40—60°), to yield 1,3-O-*benzylidene*-4-*deoxy*-L-*erythritol* (5·2 g., 58%), m. p. 84—85°, $[\alpha]_D^{18}$ −18° (*c* 1·0 in $CHCl_3$), $[M]_D$ −35° (Found: C, 68·25; H, 7·3. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%). Acetylation in the usual manner gave the O-*acetate* (74%), m. p. 51—52°, $[\alpha]_{5461}$ −50° (*c* 0·1 in $CHCl_3$), $[M]_{5461}$ −118° (Found: C, 66·85; H, 7·1. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

1,3-O-*Benzylidene*-L-*arabinitol*.—A rapid stream of hydrogen chloride was passed for 20 min. into a mixture of L-arabinitol (1·5 g.) and benzaldehyde (1·0 g.), and the mixture was stored at room temperature overnight. The hydrogen chloride was then removed as far as possible at room temperature and 0·1 mm. and final traces were removed by storage *in vacuo* over P_2O_5 and KOH. The residue was dissolved in aqueous ammonia containing sodium carbonate (0·5 g.), and the solution was extracted with light petroleum (b. p. 60—80°) to remove benzaldehyde. The product (1·66 g., 66%; m. p. 131—136°) which separated on concentration of the aqueous solution recrystallised from ethanol containing a trace of ammonia to yield 1,3-*O*-benzylidene-L-arabinitol (0·86 g.) m. p. 149—151°, $[\alpha]_D$ +7·2° (*c* 1·38 in pyridine). A further amount (0·25 g., m. p. 147—150°) was obtained from the mother liquor. Haskins *et al.*[9] record m. p. 151—152° and $[\alpha]_D$ −7·6° in pyridine for the D-isomer.

The product was readily converted by the conventional method into 2,4,5-*tri*-O-*acetyl*-1,3-O-*benzylidene*-L-*arabinitol*, m. p. 123—125°, $[\alpha]_D$ +24° (*c* 1·04 in $CHCl_3$), $[M]_D$ +88° (Found: C, 58·9; H, 6·0. $C_{18}H_{22}O_8$ requires C, 59·0; H, 6·1%).

1,3-O-*Benzylidene*-L-*threitol*.—A solution of 1,3-*O*-benzylidene-L-arabinitol (1·1 g.), sodium metaperiodate (1·1 g., 1·1 mol.) and sodium hydrogen carbonate (0·3 g.) in water was stored at room temperature for 2 hr. The solution was then extracted continuously with chloroform overnight, the extract was concentrated, yielding a syrupy residue which was dissolved in aqueous ethanol and treated with sodium borohydride (0·4 g.). After 2 hr. the solution was extracted with chloroform (6 × 30 ml.), and the extract was dried (Na_2SO_4) and concentrated. The residue (m. p. 123—127°) recrystallised from ethyl acetate–light petroleum (b. p. 60—80°), to yield 1,3-O-*benzylidene*-L-*threitol* (0·45 g.), m. p. 133—134°, $[\alpha]_D$ +8° (*c* 1·2 in pyridine), $[M]_D$ +17° (Found: C, 62·85; H, 6·85. $C_{11}H_{14}O_4$ requires C, 62·8; H, 6·7%).

The compound was readily converted by the conventional methods into its 2,4-*di*-O-*acetate*, m. p. 74—76°, $[\alpha]_D$ +43° (*c* 0·9 in $CHCl_3$), $[M]_D$ +126° (Found: C, 61·4; H, 6·2. $C_{15}H_{18}O_6$ requires C, 61·2; H, 6·2%), 2,4-*di*-O-*toluene*-p-*sulphonate* (88%), m. p. 116—118°, $[\alpha]_D$ +37° (*c* 0·6 in $CHCl_3$), $[M]_D$ +192° (Found: C, 57·9; H, 4·9; S, 12·3. $C_{25}H_{26}O_8S_2$ requires C, 57·9; H, 5·1; S, 12·4%), and 2,4-*di*-O-*methanesulphonate* (85%), m. p. 155—157°, $[\alpha]_D$ +31° (*c* 1·7 in $CHCl_3$), $[M]_D$ +113° (Found: C, 42·5; H, 5·0. $C_{13}H_{18}O_8S_2$ requires C, 42·6; H, 5·0%).

Action of Lithium Aluminium Hydride on Sulphonyl Derivatives of 1,3-O-*Benzylidene*-L-*threitol*.—(*a*) Treatment of 1,3-*O*-benzylidene-2,4-di-*O*-methanesulphonyl-L-threitol (4·4 g.) with lithium aluminium hydride (3 g.) in tetrahydrofuran (250 ml.) by essentially the method described above for the erythritol analogue gave 1,3-*O*-benzylidene-L-threitol (0·5 g., 20%), m. p. 131—133°, as the only identifiable product.

(*b*) To a stirred suspension of lithium aluminium hydride (10 g.) in tetrahydrofuran (250 ml.) was added a solution of 1,3-*O*-benzylidene-2,4-di-*O*-toluene-*p*-sulphonyl-L-threitol (14 g.) in the same solvent (50 ml.), and the mixture was boiled under reflux for 336 hr. The syrupy product (1·1 g.), isolated in the usual way, was esterified with *p*-phenylazobenzoyl chloride (3·5 g.) and pyridine (20 ml.) at 100° for 3 hr. The product, isolated in the usual manner,[17] was chromatographed on alumina. Elution with benzene–light petroleum (1 : 4 v/v) gave several zones, and the product (0·63 g.) from the main zone on rechromatography was found to contain two components of similar mobility. The leading portion of the zone gave a product of m. p. 140—155°, and the trailing portion a compound which after recrystallisation from ethanol–benzene and then benzene–light petroleum had m. p. 158—159° (Found: C, 71·5; H, 5·6; N, 7·3. $C_{24}H_{22}O_4N_2$ requires C, 71·6; H, 5·5; N, 7·0%). This compound is probably 1,3-O-*benzylidene*-4-*deoxy*-2-O-p-*phenylazobenzoyl*-L-*threitol*.

The *p*-phenylazobenzoate (50 mg.) with sodium methoxide in chloroform–methanol gave a

[17] Baggett, Foster, Haines, and Stacey, *J.* 1960, 3528.

product (21 mg.), m. p. 69—70° (from light petroleum) (Found: C, 67·9; H, 7·25. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%). The compound is probably 1,3-O-*benzylidene*-4-*deoxy*-L-*threitol*.

A solution (0·005M) of the alcohol in CCl_4 showed $\nu_{max.}$ at 3590 cm.$^{-1}$ (ε 102) for bonded hydroxyl group.[6]

Action of Sodium Benzoate in Dimethylformamide on 1,3-O-*Benzylidene*-2,4-*di*-O-*methanesulphonyl*-L-*threitol*.—A mixture of 1,3-*O*-benzylidene-2,4-di-*O*-methanesulphonyl-L-threitol (2 g.), sodium benzoate (8 g.), and dimethylformamide (100 ml.) was boiled under reflux for 6 hr., then diluted with water (100 ml.) and extracted with ether (3 × 100 ml.). The combined extracts were washed with aqueous sodium hydrogen carbonate and then water and dried (Na_2SO_4). After evaporation the residue crystallised with difficulty from aqueous ethanol. Repeated recrystallisation from this solvent mixture and finally from benzene–light petroleum gave 2,4-di-*O*-benzoyl-1,3-*O*-benzylidene-L-erythritol (76 mg., 3·5%), m. p. 85—86° alone and in admixture with the authentic compound.

Nuclear Magnetic Resonance Spectra.—The spectra were obtained at 33° from 1—1·5M-solutions in chloroform with a Mullard SL 44 mark I spectrometer at 32 Mc./sec. Peak positions were measured relative to added tetramethylsilane by graphical interpolation on a side-band "ladder" produced with a Muirhead-Wigan D 695 A decade oscillator; each shift value recorded is the mean of several measurements and is accurate to ±0·5 cycle/sec. (±0·02 p.p.m.).

The authors thank Professor M. Stacey, F.R.S., for his interest and for provision of facilities, and D.S.I.R. for a grant towards the cost of the Mullard instrument and for the award of a studentship (to J. H.).

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986. *Aspects of Stereochemistry. Part IX.* Structure of the Di-O-benzylidenetetritols.*

By A. B. FOSTER, A. H. HAINES, and J. LEHMANN.

A 1,3:2,4-distribution of the cyclic acetal rings in the di-*O*-benzylidene derivatives of erythritol and L-threitol is demonstrated by the formation of 1,3-*O*-benzylidene derivatives on graded acidic hydrolysis. Since the configuration of the monobenzylidene derivatives has been established (preceding paper) the structure of the dibenzylidene compounds may be defined completely. 1,3:2,4-Di-*O*-benzylidene-L-threitol has an "O-inside" structure. Possible effects of hydrogen bonding in the reaction of glycerol and the higher polyhydric alcohols with aldehydes are considered.

WHEREAS in the acid-catalysed reaction of pentitols and the higher polyhydric alcohols with aldehydes, six-membered cyclic acetals are formed preferentially,[1] the five-membered analogues are the predominant products in glycerol–aldehyde reactions.[2] The reaction pattern in the former group has been rationalised [3] but that of the glycerol–aldehyde series has not.[4] Since the tetritols are intermediate with respect to the above two groups of polyhydric alcohols it is surprising that there has been no report on the pattern of their reaction with aldehydes although numerous cyclic acetal derivatives are known.[1] We have now shown that, with respect to their reaction with benzaldehyde, the tetritols may be included with the higher polyhydric alcohols.

* Part VIII, preceding paper.

[1] Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.

[2] Hill, Whelen, and Hibbert, *J. Amer. Chem. Soc.*, 1928, **50**, 2235; Trister and Hibbert, *Canad. J. Res.*, 1936, **14**, *B*, 415; van Roon, *Rec. Trav. chim.*, 1929, **48**, 175.

[3] (*a*) Barker, Bourne, and Whiffen, *J.*, 1952, 3865; (*b*) Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.

[4] Brimacombe, Foster, and Haines, *J.*, 1960, 2582.

Di-*O*-benzylidene-erythritol was first described by Fischer [5] and the derivative has since been frequently used to characterise the tetritol. Graded hydrolysis of di-*O*-benzylidene-erythritol at 50° with hydrochloric acid in aqueous dioxan gave an optically inactive mono-*O*-benzylidene compound the infrared spectrum of which in Nujol or potassium chloride, or in carbon tetrachloride solution, was indistinguishable from that of 1,3-*O*-benzylidene-L-erythritol.[6] Further, the infrared spectra, in the hydroxyl stretching region,[7,8] of dilute solutions (>0·005M) of the mono-*O*-benzylidene-erythritol and 1,3-*O*-benzylidene-L-erythritol showed closely similar absorption patterns of free and intramolecularly bonded hydroxyl groups. Finally, the di-*O*-acetates of the mono-*O*-benzylidene-erythritol and 1,3-*O*-benzylidene-L-erythritol gave indistinguishable proton magnetic resonance spectra. Thus, the graded hydrolysis product may be assigned the structure 1,3-*O*-benzylidene-DL-erythritol and its precursor a 1,3:2,4-distribution of the cyclic acetal residues, on the assumption that no acetal rearrangement occurred during the graded hydrolysis.

In the preceding paper [6] 1,3-*O*-benzylidene-L-erythritol was shown to have the configuration (II); therefore 1,3:2,4-di-*O*-benzylidene-erythritol must have the bicyclic structure (I) which is related to *trans*-decalin and has two equatorial phenyl groups, a thermodynamically very stable structure. 1,3.2,4-Di-*O*-benzylidene-erythritol is an interesting example of the group of compounds which are optically inactive because of a centre of symmetry; the product of partial hydrolysis is a DL-mixfure. It is likely that other dialkylidene and diarylidene derivatives of erythritol [1] have a 1,3:2,4-distribution of the cyclic acetals.

Maquenne and Bertrand [9] first prepared di-*O*-benzylidene-D-, -L-, and -DL-threitol and these compounds have been described subsequently by other workers.[1] The di-*O*-benzylidene-L-threitol used in this work was obtained by treating benzaldehyde with L-threitol prepared from (+)-tartaric acid [10] and had m. p. 218—220° or 224—229° depending on the conditions of isolation. These modifications are probably dimorphs since they gave indistinguishable infrared spectra (KCl discs); other workers [1] have observed similar m. p. variations.

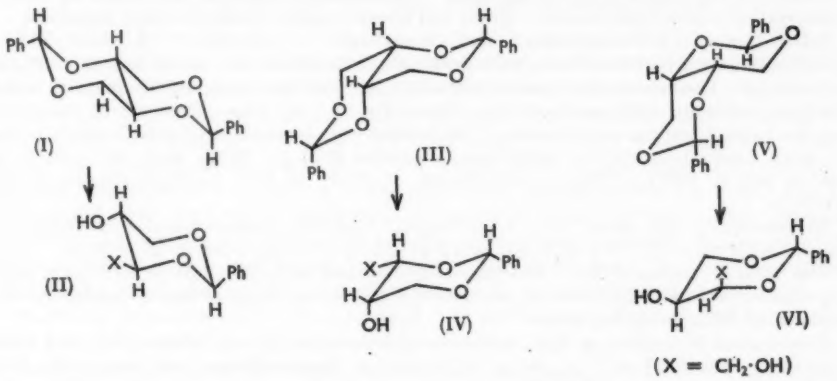
Graded hydrolysis of di-*O*-benzylidene-L-threitol with dilute hydrochloric acid in aqueous dioxan gave 1,3-*O*-benzylidene-L-threitol (IV) identical with the product obtained by periodate oxidation and subsequent borohydride reduction of 1,3-*O*-benzylidene-L-arabinitol.[6] Thus, again on the assumption that acetal migration does not occur, the di-*O*-benzylidene-L-threitol must have a 1,3:2,4-distribution of the acetal rings. Since this arrangement would form a bicyclic system related to *cis*-decalin, two structures (III) and (V), each containing chair conformations of the dioxan rings and equatorial phenyl groups, are possible for 1,3:2,4-di-*O*-benzylidene-L-threitol. Because of less adverse non-bonded interactions, the " O-inside " structure (III) should be preferred [3b] to the " H-inside " structure (V). Moreover, the products of graded hydrolysis, (IV) and (VI), respectively, of the O- and H-inside structure are different. In the preceding paper [6] 1,3-*O*-benzylidene-L-threitol was shown to have structure (IV); therefore 1,3:2,4-di-*O*-benzylidene-L-threitol must have the O-inside structure (III).

When 1,3:2,4-di-*O*-benzylidene-erythritol and 1,3:2,4-di-*O*-benzylidene-L-threitol were subjected to graded acidic hydrolysis under the same conditions, 4% of the former and 29% of the latter compound was recovered unchanged; *i.e.*, the *trans*-fused 2,4,6,8-tetraoxabicyclo[4,4,0]decane system is more easily disrupted by acid than is the *cis*-fused system. Related results have been observed with certain 4,6-*O*-benzylidenehexopyranosides.[11]

[5] Fischer, *Ber.*, 1894, **27**, 1524.
[6] Foster, Haines, Homer, Lehmann, and Thomas, preceding paper.
[7] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.
[8] Cole and Jefferies, *J.*, 1956, 4391.
[9] Maquenne and Bertrand, *Compt. rend.*, 1901, **132**, 1565.
[10] Klosterman and Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 5336.
[11] Professor W. G. Overend, personal communication.

Thus, the benzylidene acetal ring in the methyl 4,6-*O*-benzylidene-D-glucopyranosides (*trans*-fused system) is more acid-labile than is the corresponding portion of the methyl 4,6-*O*-benzylidene-D-galactopyranosides (*cis*-fused system).

Hibbert and his co-workers [2] established that, at equilibrium of the acid-catalysed reaction of glycerol with aldehydes, 1,3-dioxolan derivatives are the predominant products. This result was observed for a variety of aldehydes and it indicates that some effect is operative which reverses the usual order of thermodynamic stability of five- and six-membered rings. In contrast, at equilibrium of the acid-catalysed competition of



equimolar amounts of ethane-1,2-diol and propane-1,3-diol for an aldehyde,[2] 1,3-dioxan derivatives predominate. A parallel result has been observed in the reaction of butane-1,2,4-triol with benzaldehyde, which yields [12] 4-hydroxymethyl-2-phenyl-1,3-dioxan as the major product and only 5—10% of 4-2′-hydroxyethyl-2-phenyl-1,3-dioxolan. These results suggest that intermolecular hydrogen bonding could be important in glycerol–aldehyde reactions since the concentration of the alcohol in the reaction mixture is high. Two types of product can be formed, *viz.*, 1,3-dioxolan derivatives with free primary hydroxyl groups and 1,3-dioxan derivatives with free secondary hydroxyl groups. The greater acidity and steric accessibility of the primary hydroxyl groups might be expected to promote more efficient intermolecular hydrogen bonding than that from the secondary hydroxyl groups,[8] and this effect could counterbalance the tendency to form six-membered rings. Intermolecular hydrogen bonding would not be significant in the competition experiments and in the butane-1,2,4-triol–aldehyde reactions since, after formation of the cyclic acetals, only primary hydroxyl groups remain unsubstituted. That intermolecular hydrogen bonding is indeed involved in controlling the glycerol–aldehyde reaction is suggested by the results of preliminary experiments [13] in which the acid-catalysed reaction of benzaldehyde with glycerol was performed in an inert solvent with progressively decreasing concentrations of the reactants. As dilution increased, intermolecular hydrogen bonding diminished and it was found that, at equilibrium, the proportion of 1,3-dioxan derivatives increased and ultimately predominated. This effect is being investigated further.

Experimental

Graded Acid Hydrolysis of 1,3:2,4-*Di*-O-*benzylidene-erythritol.*—A solution of 1,3:2,4-di-*O*-benzylidene-erythritol [5] (1 g.; m. p. 201—202°) in dioxan (90 ml.) and 0·5N-hydrochloric acid (10 ml.) was kept at 50° for 45 min. The cooled solution was neutralised with aqueous ammonia

[12] Foster, Haines, and Stacey, *Tetrahedron*, in the press.
[13] Baggett and Foster, unpublished results.

and evaporated. The residue was extracted with boiling water (50 ml.); unchanged 1,3:2,4-di-*O*-benzylidene-erythritol remained. The cooled aqueous solution was extracted four times with chloroform (total 80 ml.). The combined and dried (Na_2SO_4) extracts were evaporated and the residue recrystallised from benzene–light petroleum (b. p. 60—80°), to yield 1,3-O-*benzylidene*-DL-*erythritol* (0·5 g.), m. p. 108—110°, $[\alpha]_D^{20} \pm 0°$ (*c* 1·5 in $CHCl_3$) (Found: C, 63·0; H, 6·8. $C_{11}H_{14}O_4$ requires C, 62·8; H, 6·7%). The infrared spectra of the L- and the DL-form in Nujol mulls or in CCl_4 solution were indistinguishable. The spectra obtained in KCl discs were variable, but prolonged grinding gave constant spectra which were indistinguishable.

Solutions (*ca.* 0·005M) of the L- and the DL-diol in CCl_4 had maxima at 3643, 3615, and 3565 $cm.^{-1}$ in the hydroxyl stretching region. The relative extinction coefficients for each set of absorptions were closely similar. These and related results will be discussed elsewhere.

2,4-*Di*-O-*acetyl*-1,3-O-*benzylidene*-L- *and* -DL-*erythritol*.—A mixture of 1,3-*O*-benzylidene-L-erythritol (0·24 g.), pyridine (8 ml.) and acetic anhydride (4 ml.) was stored overnight at room temperature. The mixture was poured into water, and the solution was saturated with sodium hydrogen carbonate and extracted with chloroform (3 × 50 ml.). Removal of the solvent from the extract and recrystallisation of the residue from benzene–light petroleum (b. p. 60—80°) gave 2,4-*di*-O-*acetyl*-1,3-O-*benzylidene*-L-*erythritol* (0·25 g., 74%), m. p. 81·5—83·5°, $[\alpha]_D$ −40° (*c* 0·27 in $CHCl_3$), $[M]_D$ −118° (Found: C, 61·5; H, 6·3. $C_{15}H_{18}O_6$ requires C, 61·2; H, 6·2%).

In essentially the same way 2,4-*di*-O-*acetyl*-1,3-O-*benzylidene*-DL-*erythritol* (61%) was prepared with m. p. 71—72°, $[\alpha]_D^{20} \pm 0°$ (*c* 1·5 in $CHCl_3$) (Found: C, 60·9; H, 6·3%).

The infrared spectra of the L- and the DL-di-*O*-acetate in Nujol mulls, in KCl discs, and in CCl_4 solution were indistinguishable, as were the proton magnetic resonance spectra of their solutions in $CHCl_3$ (preceding paper).[6]

Graded Acid Hydrolysis of 1,3:2,4-*Di*-O-*benzylidene*-L-*threitol*.—A solution of 1,3:2,4-di-*O*-benzylidene-L-threitol[9] (0·17 g.; m. p. 217—218°) in dioxan (20 ml.) and 0·5N-hydrochloric acid (2 ml.) was stored at 50° for 30 min. Concentrated aqueous ammonia (0·5 ml.) was then added and the mixture was evaporated to dryness. The residue, after removal of benzaldehyde in light petroleum (b. p. 60—80°), was extracted with water leaving unchanged dibenzylidene compound (*ca.* 50 mg.). The aqueous solution was added to a charcoal–Celite column (*ca.* 2 × 20 cm.). Elution with water removed inorganic material and L-threitol, and subsequent elution with aqueous alcohol (1 : 4 v/v), concentration of the eluate, and recrystallisation of the residue from benzene–light petroleum gave 1,3-*O*-benzylidene-L-threitol (6·4 mg.), m. p. 131—133° undepressed on admixture with authentic material.[6] The infrared spectrum (KCl disc) was indistinguishable from that of authentic material.

Comparative Hydrolysis of the 1,3:2,4-*Di*-O-*benzylidene Derivatives of Erythritol and* L-*Threitol*.—The di-*O*-benzylidene compounds (0·2 g.) were separately dissolved in dioxan (49 ml.), and 2·5N-hydrochloric acid (1 ml.) was added to each. The solutions were stored at 50° for 20 min., then neutralised with concentrated aqueous ammonia (0·5 ml.) and concentrated. The residue was extracted with water and the undissolved di-*O*-benzylidene compound was dried *in vacuo* over P_2O_5. In this way 4% of 1,3:2,4-di-*O*-benzylidene-erythritol (m. p. 201—202°) was recovered, and 29% of 1,3:2,4-di-*O*-benzylidene-L-threitol (m. p. 224—229°). In controls from which the acid was omitted the recovery of each di-*O*-benzylidene compound was 96—98%.

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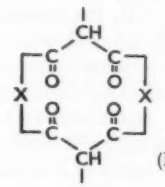
987. *Macrocyclic Bis-(1,3-diketones).*

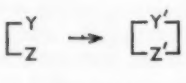
By M. M. Coombs and R. P. Houghton.

The two macrocyclic bis-(2-acetyl-1,3-diketones) (II) and (III) have been synthesised from the magnesium chelates of the αω-bis-(1,3-diketones) (IVe) and (XIe) respectively by condensation with the corresponding αω-bis(acid chlorides) in dilute solution. Other methods for the preparation of macrocyclic bis-(1,3-diketones) have been investigated, and several acyclic αω-bis-(1,3-diketones) have been obtained as intermediates or model compounds.

1,3-Diketones form stable chelate compounds having a 1 : 2 metal–ligand composition with a wide range of metals. The stability constants of many of these chelates have been measured [1] and, in general, the stability of the chelates formed by a given ligand with metals within the same group of the Periodic Table decreases with increasing atomic radius. In order to obtain a reagent which would form chelate compounds selectively with metals of a given ionic radius, it was envisaged that a compound in which two 1,3-diketone units were held rigidly apart with respect to each other would exhibit favourable properties. In other fields precedents for this concept are provided by the porphyrin pigments [2] which show a high degree of selectivity for certain metal ions, and by phthalocyanine,[3] the metal chelates of which show the maximum stability when the metal atom has an atomic radius between 1·24 and 1·43 Å. It was considered that, in the 1,3-diketone series, selectivity would be demonstrated by a macrocyclic structure of the type (I), in which X represents a suitable rigid framework. This paper describes the synthesis of two such compounds, the macrocycles (II) and (III).

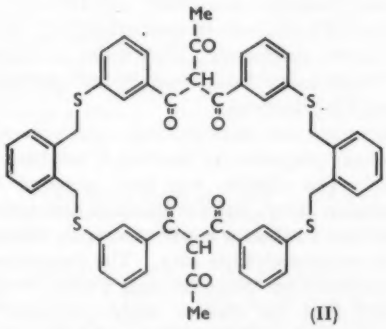


(I)

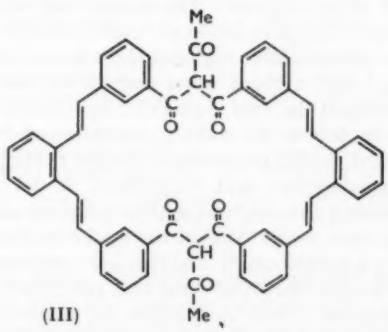


Scheme (a)

Scheme (b)



(II)



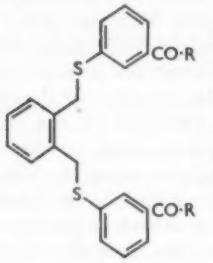
(III)

Macrocyclic compounds are usually synthesised according to the scheme (a), in which the ring is formed by joining the ends of a suitably substituted chain.[4] In the present work the alternative scheme (b) was used, and two chains bearing different reactive groups

[1] "Stability Constants," Chemical Society Spec. Publ. No. 6, London, 1957.
[2] Barnes and Dorough, *J. Amer. Chem. Soc.*, 1950, **72**, 4045.
[3] Barrett, Dent, and Linstead, *J.*, 1936, 1719.
[4] Rodd, "Chemistry of Carbon Compounds," Vol. IIA, Elsevier, London, 1953, p. 266.

were condensed to give the macrocycle. The cyclisation, which involved building the ring about a central metal atom, was carried out under the conditions normally employed for the synthesis of large ring compounds, *i.e.*, in dilute solution.[5] Aromatic 1,3-diketones of the dibenzoylmethane type were prepared because they are stronger chelating agents than the aliphatic or partly aliphatic diketones, and also because the use of aromatic nuclei presents a simple means of constructing rigid molecules.[6]

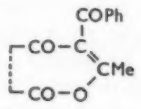
Addition of one mol. of *o*-xylylene dibromide to two mol. of the dipotassium salt of *m*-mercaptobenzoic acid[7] gave the bis(acid) (IVa), which with thionyl chloride was converted into the bis(acid chloride) (IVb). The acid chloride was treated with methanol to give the bis(methyl ester) (IVc), and with the ethoxymagnesium derivative of diethyl malonate[8] to give a tetraester, which on hydrolysis and decarboxylation afforded the bis(methyl ketone) (IVd). Base-catalysed condensation of ethyl acetate with the bis-(methyl ketone), as outlined below, gave the bis(methyl 1,3-diketone) (IVe).



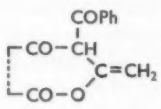
a: R = OH
b: R = Cl
c: R = OMe
d: R = Me
e: R = CH_2·COMe
f: R = CH_2·COPh

(IV)

$(Ph·CO)_2CH·COMe$ (V)



(VI)



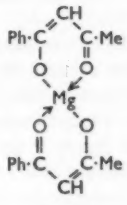
(VII)

As condensation of the bis(acid chloride) (IVb) with the bis(carbanion) derived from (IVe) appeared to be a feasible method of constructing the macrocycle (II), the following preliminary experiments were carried out. Addition of one mol. of benzoyl chloride to one of the sodium derivative of benzoylacetone, which was formed *in situ* by treatment of the diketone with triphenylmethylsodium in ether, gave an 80% yield of 1,1-dibenzoyl-acetone (V). However, when one mol. of the bis(acid chloride) (IVb) was added to two mol. of the sodium derivative, the reaction was complicated. Besides unchanged benzoyl-acetone (45% recovery), the product consisted of approximately equal parts of a neutral and an acidic gum. The former had infrared absorption bands at 1800 and 1760 (vinyl ester),[9] 1690 and 1655 cm.$^{-1}$, and probably consisted of a mixture of enol esters, *e.g.*, (VI). The alkali-soluble material showed absorption at 1790 (vinyl ester), 1715, 1695, and 1655 cm.$^{-1}$ and a broad band centred at 1600 cm.$^{-1}$ (enolised 1,3-diketone),[10] and probably contained the enol ester (VII) in addition to other 1,3-diketones.

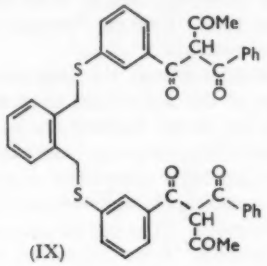
As use of the sodium derivative of benzoylacetone was unpromising, attention was turned to the magnesium chelate (VIII), which was prepared by heating a mixture of benzoylacetone and magnesium in dry benzene. The chelate was also prepared by refluxing the diketone with magnesium and ethanol in ether, but the infrared absorption spectrum indicated that the material obtained by this method was solvated with ethanol (band at 3450 cm.$^{-1}$), and this was confirmed by the microanalytical data. The magnesium chelate of benzoylacetone had previously been prepared by Weygand and Forkel,[11] who concluded (from an analysis for magnesium only) that the chelate, when prepared in ethanol, was unsolvated in contrast to the chelates formed by this diketone with the other

[5] Lüttringhaus, *Annalen*, 1937, **528**, 181; Bennett, *Trans. Faraday Soc.*, 1941, **37**, 794.
[6] Baker, McOmie, and Ollis, *J.*, 1951, 200.
[7] Stewart and Smiles, *J.*, 1921, 1792.
[8] Walker and Hauser, *J. Amer. Chem. Soc.*, 1946, **68**, 1386.
[9] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co., London, 2nd edn., 1958, p. 182.
[10] Bellamy and Beecher, *J.*, 1954, 4487.
[11] Weygand and Forkel, *J. prakt. Chem.*, 1927, **116**, 293.

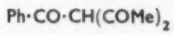
alkaline-earth metals. It now appears that their conclusion was incorrect, and was in fact based on erroneous data, for in our hands analysis of the magnesium chelates of 1,3-diketones usually gave magnesium values * which were 1—2% high. It was also found that the magnesium chelate of a 1,3-diketone could be conveniently prepared by addition of the diketone to the ethoxymagnesium derivative of diethyl malonate.



(VIII)



(IX)



(X)

Addition of the bis(acid chloride) (IVb) to a solution of the chelate (VIII) in a mixture of benzene and diethylene glycol dimethyl ether gave the bis-(2-acetyl-1,3-diketone) (IX), which was isolated as the copper chelate (40% yield). The structure of the chelate was established by analytical and molecular-weight determinations, and by the infrared absorption spectrum which showed, in addition to the carbonyl band due to six-membered chelate systems,[10] a strong band at 1645 cm.$^{-1}$. This band was found to be characteristic of the enol form of 2-acetyl-1,3-diketones and also their metal chelates (see Table 1) and

TABLE 1.

Infrared spectra of 1,3-diketones and their metal chelates.

Benzoylacetone	(1613, 1580)	1,1-Dibenzoylacetone:	
Magnesium chelate	1607, 1573, 1522	Enol form	1650 (1592, 1575, 1563)
Bis(methyl 1,3-diketone) (IVe)	(1603, 1563, 1548)	Triketo form	1705, 1671
Magnesium chelate	1592, 1562, 1508	Magnesium chelate	1646, 1592, 1572
Copper chelate	1560, 1512	Copper chelate	1640, 1580—1560vb
Bis(methyl 1,3-diketone) (XIe)	(1626, 1587), 972	1-Acetyl-1-benzoylacetone (X)	1650, 1590b
Magnesium chelate	1585, 1515, 961	Copper chelate	1640, 1560—1540vb
Copper chelate	1560, 1513, 956	Macrocycle (II)	1642, 1563b
Bis(diketone) (XIVa)	(1597, 1563)	Copper chelate	1642, 1538
Copper chelate	1587, 1546, 1515	Macrocycle (III)	1647 (1585, 1550), 960
Bis(diketone) (XIVb)	(1600, 1567)	Copper chelate	1642, 1540, 960
Copper chelate	1585, 1550, 1522	Copper chelate of (IX)	1645, 1560
Bis(diketone) (XIVc)	(1600, 1570)	Copper chelate of (XIII)	1640, 1543, 952
Copper chelate	1587, 1550, 1511b		

The maxima given are those of bands in the 1800—1500 cm.$^{-1}$ region, and those of bands due to *trans*-CH:CH groups. Figures in parentheses are the positions of the maxima of a broad composite band. All the bands are strong or very strong.

is undoubtedly due to the unchelated carbonyl group. Benzoyl chloride reacted with the chelate (VIII) to give an almost quantitative yield of 1,1-dibenzoylacetone (V); and the triketone (X) was similarly prepared from benzoyl chloride and the magnesium chelate of acetylacetone.

For the synthesis of the macrocycle (II) a 0·003M-solution in benzene and diethylene glycol dimethyl ether of equimolecular quantities of the bis(acid chloride) (IVb) and the magnesium chelate of the bis(methyl 1,3-diketone) (IVe) was kept for fourteen days at room temperature. The 1,3-diketonic material was isolated as a mixture of copper

* Magnesium was determined as the oxide by weighing the residue after the microanalysis for carbon and hydrogen.

chelates which was chromatographed on silica gel to give the copper chelate of the macrocycle contaminated with material which had infrared absorption bands at 1790 and 1730 cm.$^{-1}$. Removal of the latter material by chlorobenzene, and decomposition of the insoluble copper chelate with hydrochloric acid, gave the macrocycle (II) in 24% yield based on the magnesium chelate of the bis(methyl 1,3-diketone). The structure of the macrocycle was indicated by analytical and molecular-weight determinations, and by the infrared absorption spectrum, which in the 1500—1800 cm.$^{-1}$ region showed only the characteristic bands of the 2-acetyl-1,3-diketone systems.

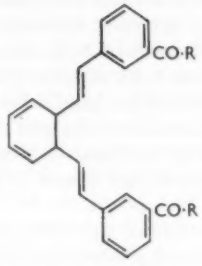
It is evident that in these condensations the magnesium fulfils two functions. It induces sufficient negative charge at the 2-positions to enable these carbon atoms to act as nucleophilic centres, and also, by firmly binding the enolic oxygen atoms, it inhibits attack upon these by the second acid chloride group before this in turn suffers condensation. After the work described above had been completed, a paper by Barry [12] appeared, in which it was shown that the action of acid chlorides on the copper chelate of a 1,3-diketone also resulted in high yields of triketones. The use of magnesium chelates for this type of reaction appears to have been confined to the acylation and aroylation of ethyl acetoacetate.[13]

Before the macrocycle was successfully synthesised as described above, attempts were made to effect the cyclisation by a double Claisen condensation between the bis(methyl ester) (IVc) and the bis(methyl ketone) (IVd). It was found that in the presence of sodium ethoxide the latter condensed smoothly with ethyl acetate, used as solvent, to give the bis(methyl 1,3-diketone) (IVe) in 60% yield. When methyl benzoate was used in place of ethyl acetate the bis(phenyl 1,3-diketone) (IVf) was obtained, as the copper chelate, in only 7% yield. In an attempt to improve the yield of the last reaction the use of sodamide in liquid ammonia, and of triphenylmethylsodium in ether as condensing agents was investigated, for it is known that the Claisen reaction between methyl ketones and aromatic esters proceeds more readily with reagents which are more nucleophilic than sodium ethoxide.[14] When these condensing agents were used, however, no pure compounds were isolated, and the 1,3-diketonic materials obtained showed strong infrared absorption bands at 1715 and 1680 cm.$^{-1}$. Condensation of the bis(methyl ketone) (IVd) with the bis(methyl ester) (IVc) under a variety of conditions failed to give 1,3-diketonic material in significant amount, and this method of effecting the cyclisation was therefore abandoned. While this work was in progress, Martin, Shamma, and Fernelius [15] described the preparation of bis-(1,3-diketones) of the type $(R{\cdot}CO{\cdot}CH_2{\cdot}CO)_2R'$, where R is aryl or alkyl and R′ arylene or alkylene, by Claisen condensation between one mol. of a diester and two mol. of a methyl ketone. Their yields were low (5—33%), thus confirming our conclusion that the double Claisen condensation is unsatisfactory for the preparation of bis-(1,3-diketones). It is interesting that Hauser and Cain [16] obtained a good yield of bis-(1,3-diketone) by condensation between 1,1′-diacetylferrocene and methyl benzoate in the presence of sodium amide in liquid ammonia, and a similar preparation of 1,4-di(acetoacetyl)benzene in 79% yield from 1,4-diacetylbenzene and ethyl acetate with powdered sodium has been described in a patent.[17]

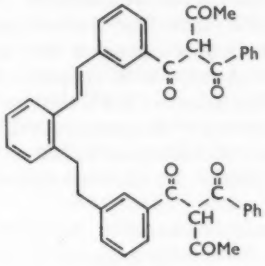
The presence of the CH_2–S linkages in the macrocycle (II) allows some flexibility, and as an example of a more rigid analogue the structure (III) was chosen because it has dimensions similar to those of the sulphur-containing macrocycle. The intermediates (XI) required for the synthesis of (III) were prepared from phthalaldehyde by an extension of the reaction recently described by Campbell and McDonald,[18] in which condensation

[12] Barry, *J.*, 1960, 670.
[13] Viscontini and Merckling, *Helv. Chim. Acta*, 1952, **35**, 2280.
[14] "Organic Reactions," Vol. VIII, John Wiley and Sons Inc., New York, 1954, p. 59.
[15] Martin, Shamma, and Fernelius, *J. Amer. Chem. Soc.*, 1958, **80**, 4891.
[16] Hauser and Cain, *J. Org. Chem.*, 1958, **23**, 1142.
[17] Wilkins and Wittbeaker, U.S.P. 2,659,711/1953.
[18] Campbell and McDonald, *J. Org. Chem.*, 1959, **24**, 1246.

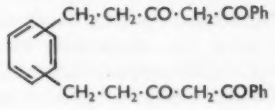
of terephthalaldehyde with the triphenylphosphonium salt of substituted benzyl bromides gave the expected *trans-trans*-distyrylbenzenes in high yield. Methyl *m*-bromomethylbenzoate [19] readily gave the triphenylphosphonium salt (XII). This (2 mol.) and phthalaldehyde (1 mol.) were treated with lithium ethoxide in ethanol. The resultant mixture of esters, upon alkaline hydrolysis, afforded a mixture of acids which was dissolved in



(XI) a : R = OH
b : R = Cl
c : R = OMe
d : R = Me
e : R = CH_2·COMe



(XIII)



(XIV) a : *ortho*
b : *meta*
c : *para*

m-$MeO_2C·C_6H_4·CH_2·\overset{+}{P}Ph_3$ Br^- (XII)

benzene containing a trace of iodine. The solution, on exposure to diffuse daylight, slowly deposited the bis(acid) (XIa) which had ultraviolet absorption maxima at 2830 and 3070 Å (ε 32,900 and 25,000 respectively). The infrared spectrum showed a strong band at 953 $cm.^{-1}$ indicative of at least one *trans*-CH:CH group, while the nuclear magnetic resonance spectrum * of the bis(methyl ester), which was obtained from the acid by treatment with diazomethane, confirmed the *trans-trans*-structure (XIc). A comparison of the infrared spectrum of the pure *trans-trans*-bis(ester) (XIc) with that of the mixture of esters obtained directly from the Wittig reaction showed that the latter material contained very little of the *trans-trans*-bis(ester), and it therefore appears that this reaction is an exception to the general rule that double bonds formed in the Wittig reaction have predominantly the *trans*-configuration.[20]

The bis(acid) (XIa) was converted into the bis(acid chloride) (XIb), the bis(methyl ketone) (XId), and the bis(methyl 1,3-diketone) (XIe) by the methods used in the other series. The bis(acid chloride) (XIb) reacted with the magnesium chelate of benzoylacetone to give the bis-(2-acetyl-1,3-diketone) (XIII), and with methanol to give the bis(methyl ester) (XIc) which was identical with that prepared from the acid (XIa) by treatment with diazomethane. Condensation of the magnesium chelate of the bis(methyl 1,3-diketone) (XIe) with the bis(acid chloride) (XIb) in a dilute solution of benzene and dioxan gave a mixture from which the macrocycle (III) was isolated, by means of the copper chelate, in 21% yield.

In an attempt to prepare other types of bis-(1,3-diketones) condensation of the dianion of benzoylacetone with dihalogen compounds was studied, the conditions described by Harris and Hauser [21] for the alkylation of 1,3-diketones with benzyl chloride being used. Addition of one mol. of *o*-, *m*-, or *p*-xylylene dibromide to two mol. of benzoyl acetone and four equivalents of potassium amide in liquid ammonia gave the corresponding bis-(1,3-diketones) (XIV) in 15—25% yield. These bis(diketones) formed monomeric 1 : 1 chelates with copper, indicating that the side chains are sufficiently flexible to allow the

* Bands due to olefinic protons at 3·70 and 2·89 (J = 16·2 cycles/sec.), expressed as τ values, as defined by Tiers (*J. Phys. Chem.*, 1958, **62**, 1151). We are indebted to Dr. D. T. Thompson of this Department for recording and interpreting the spectrum.

[19] Fuson and Cook, *J. Amer. Chem. Soc.*, 1940, **62**, 1180.
[20] Trippett, *Adv. Org. Chem.*, 1960, **1**, 83.
[21] Harris and Hauser, *J. Amer. Chem. Soc.*, 1958, **80**, 6360.

two 1,3-diketone groups to chelate with the same copper atom. Similar condensations between the dianion of acetylacetone and the three isomeric xylylene dibromides gave 1,3-diketonic oils from which no pure compounds could be isolated.

All the bis-(1,3-diketones) described in this paper are very largely enolised, as indicated by their infrared absorption spectra which show the broad band between 1500 and 1600 cm.$^{-1}$ characteristic of the hydrogen-bonded chelate system.[10] Models of these compounds, except those of the bis(diketones) (XIV), show that the four oxygen atoms of the enolised 1,3-diketone systems lie at the corners of a square of side approximately 3 Å, and as expected the compounds form 1 : 1 chelates with copper. In the infrared absorption spectra of the copper chelates, including those of (XIV), the broad absorption band between 1500 and 1600 cm.$^{-1}$ present in the spectra of the parent 1,3-diketones is usually split into several strong bands, but the absence of additional carbonyl absorption bands indicates that the four oxygen atoms of the enolised 1,3-diketone systems are firmly bound to the metal.

The stability constants of the chelates formed by the macrocycles (II) and (III), and by the bis-(1,3-diketones) (IVe) and (XIV) with magnesium, calcium, and strontium were kindly measured by Professor G. Schwarzenbach and Dr. G. Anderegg of the Eidg. Technische Hocnschule, Zürich, and we are most grateful to them for the figures given in Table 2 and for the following interpretation of their results. The data confirm that the compounds examined were bis-(1,3-diketones), the values of pK_2 being only slightly lower than those of pK_1. In the compounds (IVe) and (XIV) the first proton leaves the molecule at approximately the same pH as in acetylacetone, but the macrocycles (II) and (III) are more acidic than acetylacetone, possibly owing to electron withdrawal by the acetyl groups. (A similar comparison may be made between acetylacetone and 1,1-diacetylacetone, for which the pK values in aqueous solution are 8·9 and 5·9 respectively.[22]) Presumably for the same reason, the chelates of the macrocycles are less

TABLE 2.

Stability constants of the chelates of bis-(1,3-diketones).

All values were obtained by Dr. G. Anderegg from titrations with a glass electrode in 1 : 3 (v/v) water–dioxan at 20°, and an ionic strength (I = 0·1) kept constant by sodium perchlorate. L^{2-} denotes the ligand anion obtained by removing two protons from one molecule of the bis(diketones) or from two molecules of acetylacetone.

$$K_{HL^-} = [HL^-]/[H^+][L^{2-}];\ K_{H_2L} = [H_2L]/[H^+][HL^-];\ K_{ML} = [ML]/[M^{2+}][L^{2-}];$$
$$K_{MHL^+} = [MHL^+]/[M^{2+}][HL^-].$$

Square brackets denote concentrations in mole l.$^{-1}$.

Compound	log K_{HL^-} = pK_1	log K_{H_2L} = pK_2	log K_{ML} Mg	log K_{ML} Ca	log K_{ML} Sr	log K_{MHL^+} Mg	log K_{MHL^+} Ca	log K_{MHL^+} Sr
(II)	8·44	7·64	6·65	5·35	4·19	4·07	3·27	2·58
(III)	8·88	8·36	8·00	6·61	5·14	4·20	3·24	2·77
(IVe)	10·31	10·52	9·27	6·75	5·31	5·73	4·46	3·43
(XVa)	10·76	10·68	8·12	5·98	4·68	5·46	4·16	3·27
(XVb)	10·91	10·43	9·08	6·86	5·41	5·15	3·90	3·11
(XVc)	11·09	10·45	—	—	—	5·12	4·14	3·32
Acetylacetone ...	10·67	—	5·23	4·11	3·32	—	—	—

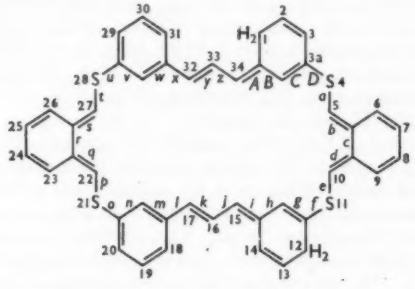
stable than those of the acyclic bis-(1,3-diketones). The stability of the chelates of all the compounds examined shows the usual order Mg > Ca > Sr. The difference between the stability constants of the magnesium chelates of the macrocycles and of the acyclic bis-(1,3-diketones) is greater than the corresponding differences for the calcium and strontium chelates, which suggests that the steric requirements of the larger cations (Ca^{2+}, ionic radius 0·99 Å; Sr^{2+}, 1·13 Å) [23] are met slightly better than those of the smaller magnesium ion (ionic radius, 0·65 Å) [23] by both macrocycles; however, the initial object of constructing a specific chelating agent has not been realised.

[22] Schwarzenbach and his co-workers, unpublished work.
[23] Pauling, *J. Amer. Chem. Soc.*, 1927, **49**, 765.

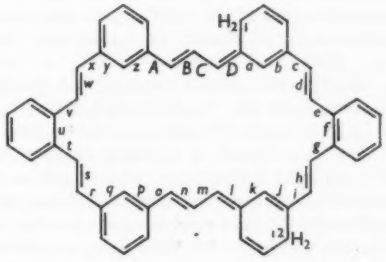
The chelates of both the acyclic and the macrocyclic bis-(1,3-diketones) are more stable than those of acetylacetone, indicating that the presence of a second 1,3-diketone group in these compounds helps to stabilise their chelates. Of the three isomeric bis-(1,3-diketones) (XIVa, b, and c) the *meta*- appears to be more favourable than the *ortho*-structure for the formation of chelates; the results for the *para*-compound were inconsistent, probably because of the formation of chelates which did not have a 1 : 1 metal–ligand composition. In this connection it was observed that only a very poor yield of the 1 : 1 copper chelate of the *para*-compound was obtained under conditions which readily gave good yields of the copper chelates of the *ortho*- and the *meta*-isomer.

All the bis-(1,3-diketones) examined also formed chelates of the type (MHL^+), in which only one of the 1,3-diketone groups is bound to the metal, the other group retaining its proton. As expected, the chelates of this type formed by the macrocycles were less stable than the corresponding chelates of the acyclic bis-(1,3-diketones), while the latter were about as stable as those of the type (ML) formed by acetylacetone. From titrations which were run in the presence of an excess of metal it appeared that chelates of the type (M_2L^{2+}), in which the two 1,3-diketone groups are bound to different metal atoms, were not formed to an appreciable extent, except possibly with compound (XIVc).

Note on Nomenclature.—Systematic names for the macrocycles (II) and (III) are formed from cyclotriacontane with benzo-ring fusion, in accordance with the principles of the Ring Index,[24] the " ane " ending being replaced by " in " to denote the " least hydrogenated " forms (IIa) and (IIIa); the " extra " (indicated) hydrogen atom is allotted to the position carrying the lowest number in the finally numbered molecule. When the ring-fusions are denoted, the Ring Index principle is extended beyond *a*—*z* by using capital letters; the lettering begins at a sulphur atom in (IIa) and at a fused benzene ring in (IIIa). We thank the Editors for assistance in naming these compounds.



(IIa)



(IIIa)

Experimental

Microanalyses were by Miss J. Cuckney and the staff of the Organic Microanalytical Laboratory. Molecular weights were determined by the ebullioscopic method (in chlorobenzene). Infrared spectra were obtained with samples prepared as Nujol mulls. Unless stated to the contrary, light petroleum refers to the fraction of b. p. 40—60°.

m-*Mercaptobenzoic Acid.*—Benzoic acid was converted successively into *m*-chlorosulphonylbenzoic acid, di-(*m*-carboxyphenyl) disulphide, and *m*-mercaptobenzoic acid by Stewart and Smiles's procedure.[7] The acid, which was obtained in an overall yield of 22%, had m. p. 140—143° (lit.,[7] m. p. 146—147°), and was used without further purification.

o-*Phenylenedi-*[(m-*methylenethio*)*benzoic Acid*] (IVa).—Potassium hydroxide (40·1 g.) in water (30 ml.) was added to *m*-mercaptobenzoic acid (111 g.) in ethanol (450 ml.) under nitrogen. *o*-Xylylene dibromide (96 g.) in chloroform (450 ml.) was added with stirring during 2 hr. The mixture was stirred and heated under reflux for a further 2 hr. and the solvent was then removed

[24] " The Ring Index," American Chemical Society, Washington, 1959, 2nd edn., p. xxii.

XUM

under reduced pressure. The residue was dissolved in 1·25N-sodium hydroxide (700 ml.), and this solution was extracted with chloroform. The aqueous layer was filtered then acidified with concentrated hydrochloric acid, to give the *bis(acid)* (113 g.) as a granular solid, m. p. 217—224°. A sample crystallised from ethanol as needles, m. p. 227—228° (Found: C, 63·8; H, 4·25; S, 15·2. $C_{22}H_{18}O_4S_2$ requires C, 64·0; H, 4·5; S, 15·3%).

The bis(acid) (1·0 g.) was boiled under reflux with acetic acid (50 ml.) containing 30% hydrogen peroxide (10 ml.) for 3 hr. and cooled. o-*Phenylenedi*-[(m-*methylenesulphonyl*)-*benzoic acid*] *monohydrate* separated as needles (0·96 g.), m. p. 297—300°; the analytical sample was dried at 100° *in vacuo* (Found: C, 53·7; H, 4·3; S, 13·05. $C_{22}H_{18}O_8S_2,H_2O$ requires C, 53·65; H, 4·1; S, 13·05%).

o-*Phenylenedi*-[(m-*methylenethio*)*benzoyl Chloride*] (IVb).—The bis(acid) (104 g.) was boiled with thionyl chloride (500 ml.) for 2 hr. The excess of reagent was removed under reduced pressure and the residual oil was extracted with hot light petroleum (b. p. 60—80°; 8 × 250 ml.). The extracts were cooled to give the *bis(acid chloride)* (80·5 g.) as needles, m. p. 72—74° (Found: C, 58·8; H, 4·3; Cl, 16·05; S, 4·2. $C_{22}H_{16}Cl_2O_2S_2$ requires C, 59·05; H, 3·6; Cl, 15·85; S, 4·3%).

The bis(acid chloride) (1·0 g.) was refluxed with dry methanol (25 ml.) for 2 hr. On cooling, the solution gave *dimethyl* o-*phenylenedi*-[(m-*methylenethio*)*benzoate*] (IVc) (0·9 g.), m. p. 76—77° (Found: C, 65·55; H, 5·4; S, 14·5. $C_{24}H_{22}O_4S_2$ requires C, 65·7; H, 5·05; S, 14·6%).

o-*Phenylenedi*-[(m-*methylenethio*)*acetophenone*] (IVd).—Magnesium turnings (2·7 g.) were allowed to react with absolute ethanol (2·5 ml.) containing carbon tetrachloride (0·25 ml.). After the initial reaction had subsided the mixture was diluted with dry ether (75 ml.), and diethyl malonate (17 ml.) in absolute ethanol (10 ml.) and dry ether (15 ml.) was added dropwise during 30 min. The mixture was stirred and refluxed for a further 3½ hr. by which time only a trace of magnesium remained. To 25 ml. of this solution was added with stirring the bis(acid chloride) (IVb) (4·47 g.) in ether (25 ml.) and carbon tetrachloride (10 ml.). The mixture was heated under reflux for 3½ hr., cooled, and decomposed with cold 5N-sulphuric acid. The organic layer was washed with water and evaporated, to yield an amber-coloured syrup which was heated under reflux for 6 hr. with water (10 ml.), acetic acid (15 ml.), and concentrated sulphuric acid (2 ml.). The product, which solidified on cooling, was collected, washed with water, and crystallised from butan-1-ol, to give the *bis(methyl ketone)* (3·22 g.), m. p. 141—141·5°, $\nu_{max.}$ 1670 cm.$^{-1}$ (Found: C, 70·6; H, 5·3; S, 15·5. $C_{24}H_{22}O_2S_2$ requires C, 70·9; H, 5·45; S, 15·8%); this gave a *bis*-(2,4-*dinitrophenylhydrazone*), m. p. 224° (decomp.) (Found: C, 56·25; H, 4·2; N, 14·95. $C_{36}H_{28}N_8O_8S_2$ requires C, 56·55; H, 3·7; N, 14·65%).

o-*Phenylenedi*-[(m-*methylenethio*)*acetoacetylbenzene*] (IVe).—The bis(methyl ketone) (IVd) (7·45 g.), suspended in dry ethyl acetate (300 ml.), was added to sodium ethoxide (from sodium, 1·75 g.), and the mixture was stirred and heated under reflux for 4 hr. After being cooled, the mixture was added to water (50 ml.) at 0°, the organic layer was extracted with 0·2N-sodium hydroxide (50 ml.), and the extract was added to the aqueous layer. The combined aqueous solution was kept at 0° for 5 min., and the solid which separated was collected, washed with dry ether (20 ml.), and suspended in water (50 ml.). The suspension was acidified with concentrated hydrochloric acid, and the organic material was extracted with ether to yield material (5·43 g.) of m. p. 65—67°. Crystallisation from methanol gave pale yellow prisms of the *bis(methyl* 1,3-*diketone*), m. p. 72—73° (Found: C, 68·25; H, 5·45; S, 13·3. $C_{28}H_{26}O_4S_2$ requires C, 68·55; H, 5·35; S, 13·1%).

This compound, in ether, was shaken with aqueous cupric acetate to give the *copper chelate*, which crystallised from chloroform–light petroleum as bright green needles, m. p. 202—204° (Found: C, 60·8; H, 4·75%; *M*, 570. $C_{28}H_{24}CuO_4S_2$ requires C, 60·65; H, 4·3%; *M*, 554).

o-*Phenylenedi*-[(m-*methylenethio*)*benzoylacetylbenzene*] (IVf).—Sodium ethoxide (from sodium, 0·45 g.) was heated at 160°/0·5 mm. for 2 hr. The flask was filled with dry nitrogen, and methyl benzoate (20 ml.) and the bis(methyl ketone) (IVd) (2·0 g.) were introduced, and a condenser was arranged so that methanol formed during the reaction would distil off. The mixture was stirred and heated at 120° for 1½ hr. under dry nitrogen, cooled, diluted with ether, and extracted with aqueous sodium hydroxide. The aqueous solution was acidified with dilute sulphuric acid, and the liberated oil was extracted with ether. The extract was washed with sodium hydrogen carbonate solution and shaken with aqueous cupric acetate to give a dark green, sticky solid (1·0 g.), which was collected and dissolved in chloroform (100 ml.). Gradual addition of light petroleum caused the separation, in three crops (0·19 g., 0·18 g., and

0·05 g.), of a pale green microcrystalline solid which recrystallised from chloroform–light petroleum to give the *copper chelate* of the bis(phenyl-1,3-diketone) (IVf) as green prisms, decomp. 245° (Found: C, 65·3; H, 4·5; S, 9·3. $C_{38}H_{28}CuO_4S_2,H_2O$ requires C, 65·7; H, 4·35; S, 9·2%).

When the above condensation was carried out in liquid ammonia (30 ml.) containing sodamide (from sodium, 0·6 g.) according to Hauser and Cain's method,[16] the alkali-soluble product was an orange oil (0·4 g.) which showed strong infrared absorption bands at 1715, 1681, and 1563 (broad) cm.$^{-1}$. With aqueous cupric acetate the oil gave a yellowish-green solid which darkened but did not melt below 320°.

A similar result was obtained with triphenylmethylsodium in ether–benzene, and no crystalline material was obtained.

Reactions with the Sodium Derivative of Benzoylacetone.—(a) 1,1-*Dibenzoylacetone.* Ethereal 0·10N-triphenylmethylsodium solution [25] (45·3 ml., 5 millimoles) was quickly added with stirring to benzoylacetone (0·811 g., 5 millimoles) in dry ether (50 ml.) under dry nitrogen, followed by a mixture of benzoyl chloride (0·703 g., 5 millimoles) and ether (20 ml.) during 15 min. at 20°. After 2 hr. water was added and the material soluble in aqueous sodium hydroxide but insoluble in sodium hydrogen carbonate solution was isolated (1·06 g.; m. p. 79—85°). Recrystallisation from light petroleum (b. p. 80—100°) gave prisms of 1,1-dibenzoylacetone (0·68 g.), m. p. 81—83° (lit.,[26] m. p. 80—85°).

(b) *Reaction with the bis(acid chloride)* (IVb). Benzoylacetone (0·972 g., 6 millimoles) in ether (60 ml.) was treated with ethereal triphenylmethylsodium (6 millimoles) as before. A solution of the bis(acid chloride) (IVb) (1·331 g., 3 millimoles) in benzene (50 ml.) was added dropwise during 15 min., and stirring was continued at room temperature for 4 hr. Water was added and the product was separated into a neutral fraction (2·32 g.) and a fraction (1·04 g.) which was soluble in aqueous sodium hydroxide. The former was extracted with hot light petroleum to remove triphenylmethane and evaporated to yield a resin (0·46 g.) which had strong infrared absorption bands at 1800, 1760, 1690, and 1655 cm.$^{-1}$. The fraction soluble in alkali was also extracted repeatedly with light petroleum, and from the extracts was recovered benzoylacetone (0·44 g.), m. p. 52—54°, raised to 54—56° when mixed with an authentic sample, m. p. 60—61°. The residue, an amber-coloured gum (0·55 g.), had infrared absorption bands at 1790, 1715, 1695, 1655, and 1570 (broad) cm.$^{-1}$. No crystalline materials were obtained from the petroleum-insoluble fractions.

Magnesium Chelate of Benzoylacetone (VIII).—(*a*) A mixture of benzoylacetone (3·24 g.), magnesium (0·27 g.), and dry benzene (15 ml.) was refluxed for 65 hr. The suspension was decanted from the unchanged magnesium, and filtered to give the *chelate* (2·02 g., 58%), m. p. 282—283° (Found: C, 69·55; H, 5·55. $C_{20}H_{18}MgO_4$ requires C, 69·3; H, 5·2%).

(*b*) Benzoylacetone (6·21 g.) in dry ethanol (25 ml.) and dry benzene (25 ml.) was added dropwise during 15 min. to a boiling suspension of magnesium (0·46 g.) in dry ethanol (50 ml.). The mixture was refluxed for a further 1 hr., then filtered and concentrated under reduced pressure to about 25 ml. The solid which separated was washed with cold benzene (10 ml.) to leave the solvated *chelate* (6·33 g., 91%), m. p. 278—279° raised to 281—282° by one recrystallisation from ethanol–benzene (Weygand and Forkel [11] give m. p. "about 267°") [Found: C, 66·9; H, 6·1%; *M*, 736. $(C_{20}H_{18}MgO_4)_2,2EtOH$ requires C, 67·3; H, 6·2%; *M*, 784]. The infrared absorption spectrum was almost identical with that of the sample described above, but showed an additional band at 3450 cm.$^{-1}$ (OH stretching).

1,1-*Dibenzoylacetone* (V) *from the Magnesium Chelate.*—A cooled solution of the magnesium chelate (471 mg.) of benzoylacetone in diethylene glycol dimethyl ether (5 ml.) was diluted with dry benzene (50 ml.), treated with benzoyl chloride (0·80 ml.), kept at room temperature for 21 hr., and shaken with N-hydrochloric acid (10 ml.). The organic layer was extracted with 0·2N-sodium hydroxide (2 × 25 ml.), and the extracts were acidified with 2N-hydrochloric acid. Extraction with ether afforded a product (619 mg.), m. p. 70—75°, which was recrystallised from light petroleum (b. p. 80—100°) to give the enol form of 1,1-dibenzoylacetone (516 mg., 81%), m. p. 79—82°, partly solidifying at 90—95°, then remelting at 101—105°. The triketo-form, m. p. 109—110°, was obtained as needles by slowly recrystallising a sample of the enol form from ethanol (Claisen [26] gives m. p.s 80—85° and 107—110° for the enol and the triketo-form respectively).

[25] *Org. Synth.*, Collective Vol. II, John Wiley and Sons, Inc., New York, 1943, p. 607.
[26] Claisen, *Annalen*, 1896, **291**, 75.

XUM

Addition of the triketone (enol form, 2·66 g.) in benzene (15 ml.) to a boiling suspension of magnesium (0·12 g.) in dry ethanol (10 ml.) gave the *magnesium chelate* (2·66 g., 96%) which crystallised from 2-ethoxyethanol as a yellow powder, m. p. 275° (Found: C, 73·5; H, 5·2. $C_{34}H_{26}MgO_6$ requires C, 73·6; H, 4·7%).

Copper Chelate of o-*Phenylenedi*-[(m-*methylenethio*)-α-*benzoylacetylbenzene*] (IX).—The bis-(acid chloride) (IVb) (1·72 g.) in dry benzene (100 ml.) was added to the magnesium chelate (1·33 g.) of benzoylacetone in diethylene glycol dimethyl ether (25 ml.), and the mixture was kept at room temperature for 36 hr. Isolation of the 1,3-di-ketonic material in the usual way afforded an orange gum (1·89 g.) which was shaken in ether (25 ml.) with saturated aqueous cupric acetate (20 ml.). The solid which separated was collected and recrystallised from chloroform–light petroleum to give the *copper chelate* (1·03 g., 40%), m. p. 190—192° raised to 198—199° when chromatographed on silica gel in chloroform (Found: C, 66·4; H, 4·7; S, 8·8%; *M*, 724. $C_{42}H_{32}CuO_6S_2$ requires C, 66·3; H, 4·25; S, 8·45%; *M*, 760).

3-*Benzoylpentane*-2,4-*dione* (X) *from the Magnesium Chelate of Acetylacetone*.—Acetylacetone (14·8 g.) in dry ethanol (100 ml.) was added dropwise during 30 min. to a boiling suspension of magnesium (2·0 g.) in dry ethanol (20 ml.). The mixture was refluxed for a further 2 hr. and then filtered and cooled to give the chelate (10·0 g., 61%) as needles, m. p. 269—270° (decomp.) (Found: C, 53·9; H, 6·3. Calc. for $C_{10}H_{14}MgO_4$: C, 53·9; H, 6·35%) (Hatch and Sutherland [27] give m. p. 265—267°). A solution of the chelate (1·75 g.) in hot diethylene glycol dimethyl ether (25 ml.), was cooled and diluted with dry benzene (100 ml.). Benzoyl chloride (1·82 g.) was added and the mixture was kept at room temperature for 20 hr. Isolation of the 1,3-diketonic material gave an oil (2·34 g.) which was dissolved in light petroleum (10 ml.). The solution was kept at 0° for 24 hr. to give the enol form of the triketone (1·84 g., 70%) as prisms, m. p. 31—31·5° (lit.,[28] m. p. 35°). The copper chelate crystallised from dioxan as light blue plates, m. p. 230—231° (decomp.) (lit.,[28] m. p. 224—225°).

Magnesium Chelate of o-*Phenylenedi*-[(m-*methylenethio*)*acetoacetylbenzene*].—(*a*) Treatment of the bis(methyl 1,3-diketone) (IVe) (3·50 g.) in dry benzene (25 ml.) with magnesium (0·73 g.) in dry ethanol (20 ml.) according to the usual method gave the *chelate* (2·37 g., 59%), m. p. 190—193° raised to 195—196° by one recrystallisation from ethanol–chlorobenzene (Found: C, 64·2; H, 5·2%; *M*, 555. $C_{28}H_{24}MgO_4S_2$,EtOH requires C, 64·5; H, 5·4%; *M*, 559).

(*b*) Diethyl malonate (6·1 g.) in dry dioxan (30 ml.) was added dropwise to a boiling suspension of magnesium (0·93 g.) in dry ethanol (5 ml.). The mixture was refluxed for a further 30 min., then cooled and diluted with dry ether (100 ml.). The bis(methyl 1,3-diketone) (IVe) (18·7 g.) in dry benzene (50 ml.) was added, and after 30 min. the mixture was filtered and concentrated under reduced pressure to give the chelate (15·0 g., 70%), m. p. 188—190°, which had an infrared absorption spectrum identical with that of the sample described above.

16,33-*Diacetyl*-5,10,16,17,22,27,33,34-*octahydro*-15,32H-*hexabenzo*[c, gh, mn, r, vw, BC] [1,6,16,21]*tetrathiacyclotriacontin*-15,17,32,34-*tetraone* (II).—The magnesium chelate (6·38 g.) of the bis(methyl 1,3-diketone) (IVe) was dissolved in diethylene glycol dimethyl ether (150 ml.), and the solution was diluted with dry benzene (4 l.). The bis(acid chloride) (IVb) (5·15 g.) in dry benzene (100 ml.) was added and the mixture was kept at room temperature for 14 days. The benzene was removed under reduced pressure and the residual solution was shaken vigorously for 5 min. with a mixture of chloroform (250 ml.), ice (200 g.), and concentrated hydrochloric acid (40 ml.). The chloroform layer was separated, washed with water (2 × 250 ml.), and evaporated under reduced pressure, to give a solid. This was shaken in chloroform (500 ml.) with aqueous cupric acetate (5 g. in 200 ml.), and the chloroform layer was separated, concentrated under reduced pressure to about 350 ml., and added to a column of acid-washed silica gel (500 g.). The column was developed with chloroform, and the main band was eluted and evaporated to give a solid which was extracted with hot benzene (4 × 50 ml.) and boiling chlorobenzene (25 ml.); this left the crude copper chelate (3·44 g., 32%) of the macrocycle (II) as a green solid, m. p. >340°, which could not be satisfactorily purified (Found: C, 63·7; H, 4·3; S, 14·55. Calc. for $C_{50}H_{32}CuO_6S_4$: C, 64·8; H, 4·15; S, 13·85%). A suspension of the chelate (3·44 g.) in chloroform (50 ml.) was shaken with concentrated hydrochloric acid (50 ml.) at 0°. The organic layer was washed with water, and chlorobenzene (50 ml.) was added. The chloroform was removed under reduced pressure, the residual chlorobenzene solution was heated to the b. p., and hot ethanol (100 ml.) was added. The *macrocycle* (2·44 g., 76%) which

[27] Hatch and Sutherland, *J. Org. Chem.*, 1948, **13**, 249.
[28] Claisen, *Annalen*, 1893, **277**, 200.

slowly crystallised from the solution had m. p. 198—200°, raised to 208—209° by two recrystallisations from chlorobenzene–ethanol (Found: C, 69·5; H, 4·9; S, 14·8%; *M*, 813. $C_{50}H_{40}O_6S_4$ requires C, 69·4; H, 4·7; S, 14·8%; *M*, 865).

m-*Methoxycarbonylbenzyltriphenylphosphonium Bromide* (XII).—A solution of methyl *m*-bromomethylbenzoate [19] (55 g.) and triphenylphosphine (100 g.) in xylene (500 ml.) was stirred and refluxed for 5 hr. The solid which separated was washed with ether and dried at 60°, to give the *salt* (109 g., 92%), m. p. 221—223°, raised to 225—226° by one recrystallisation from ethanol (Found: C, 64·65; H, 5·8; Br, 14·9. $C_{27}H_{24}BrO_2P$,EtOH requires C, 64·8; H, 5·6; Br, 14·7%).

trans-trans-o-*Phenylenedi*-(m-*vinylidenebenzoic acid*) (XIa).—Lithium ethoxide (from lithium, 70 mg.) in ethanol (100 ml.) was added to a solution of phthalaldehyde [20] (0·50 g.) and the phosphonium salt (XII) (5·0 g.) in ethanol (50 ml.). The mixture was kept at room temperature for 6 hr., then diluted with water (200 ml.). Extraction with chloroform (30 ml., 10 ml.) yielded a viscous oil which was refluxed for 4 hr. with sodium hydroxide (0·70 g.) in methanol (50 ml.) and water (15 ml.). The bulk of the methanol was removed under reduced pressure and the aqueous residue was extracted with ether and acidified. Extraction with chloroform afforded a gum (1·74 g.) which was dissolved in benzene (30 ml.) and ether (30 ml.) containing iodine (20 mg.) and illuminated with diffuse daylight. The *acid* (1·05 g., 75%) which slowly separated had m. p. 272—274° raised to 277—278° by one recrystallisation from aqueous dimethylformamide (Found: C, 77·6; H, 4·9. $C_{24}H_{18}O_4$ requires C, 77·8; H, 4·9%), $\lambda_{max.}$ 2830 and 3070 Å (ε 32,900 and 25,000 respectively) in dioxan.

trans-trans-o-*Phenylenedi*-(m-*vinylidenebenzoyl Chloride*) (XIb).—A mixture of the bis-(acid) (XIa) (4·61 g.) and thionyl chloride (15 ml.) was refluxed for 3 hr. The excess of the reagent was removed under reduced pressure and the residue was recrystallised from carbon tetrachloride–light petroleum (b. p. 60—80°), to give the *bis(acid chloride)* (3·70 g., 73%) as a pale yellow solid, m. p. 114—115°. A sample of m. p. 118—119° was obtained by recrystallisation from benzene–light petroleum (b. p. 80—100°) (Found: C, 70·3; H, 4·3. $C_{24}H_{16}Cl_2O_2$ requires C, 70·8; H, 4·0%).

trans-trans-o-*Phenylenedi*-(m-*vinylidene-α-benzoylacetoacetylbenzene*) (XIII).—The bis(acid-chloride) (XIb) (548 mg.) in dry benzene (30 ml.) was added to the magnesium chelate (511 mg.) of benzoylacetone in diethylene glycol dimethyl ether (10 ml.) and dry benzene (60 ml.). After 40 hr. the 1,3-diketonic material was isolated as a viscous oil (740 mg.) which was treated with aqueous cupric acetate in the usual way. The product was chromatographed on silica gel in chloroform, and recrystallised from dioxan to give the *copper chelate* (140 mg., 14%) as a light green solid, m. p. 298—299° (Found: C, 73·4; H, 4·6; Cu, 8·6%; *M*, 729. $C_{44}H_{32}CuO_6$ requires C, 73·35; H, 4·5; Cu, 8·6%; *M*, 720). Treatment of the chelate (140 mg.) in chloroform (10 ml.) with N-hydrochloric acid (10 ml.) gave the *bis-(1,3-diketone)* (115 mg., 90%) as a glass (Found: C, 80·0; H, 5·6. $C_{44}H_{34}O_6$ requires C, 89·2; H, 5·2%).

Dimethyl trans-trans-o-*Phenylenedi*-(m-*vinylidenebenzoate*) (XIc).–(*a*) A suspension of the bis(acid chloride) (XIb) (215 mg.) in methanol (20 ml.) was refluxed for 2 hr. The methanol was removed under reduced pressure and the residue was washed with carbon tetrachloride (25 ml.) to leave the *bis(methyl ester)* (175 mg., 83%) as plates, m. p. 161—162° (Found: C, 78·0; H, 5·8. $C_{26}H_{22}O_4$ requires C, 78·4; H, 5·6%), $\lambda_{max.}$ 2460, 2830, and 3160 Å (ε 22,900, 39,700, and 28,300 respectively) in dioxan.

(*b*) A suspension of the bis(acid) (XIa) (208 mg.) in tetrahydrofuran (10 ml.) was treated with an excess of ethereal diazomethane. After 2 hr. the mixture was washed with 0·5N-sodium hydroxide and evaporated under reduced pressure to leave a solid (163 mg., 73%), m. p. 159—160°, which had an infrared absorption spectrum identical with that of the sample described above.

trans-trans-o-*Phenylenedi*-(m-*vinylideneacetophenone*) (XId).—Diethyl malonate (6·0 g.) in dry dioxan (45 ml.) was added dropwise during 20 min. to a boiling suspension of magnesium (0·92 g.) in dry ethanol (10 ml.). The mixture was refluxed for a further 1 hr., cooled and diluted with ether (50 ml.). The bis(acid chloride) (XIb) (6·28 g.) in dioxan (45 ml.) was added during 15 min. and the mixture was stirred and refluxed for 4 hr., then shaken with 2N-sulphuric acid (50 ml.) at 0°. The organic layer was separated, and the oil obtained by removal of the solvent was refluxed for 6 hr. in water (20 ml.), acetic acid (40 ml.), and sulphuric acid (6 ml.). The product was filtered off, washed with water (200 ml.), and recrystallised once from butan-1-ol

[20] Bill and Tarbell, *Org. Synth.*, 1954, **34**, 82.

to give the *bis(methyl ketone)* (3·14 g., 50%), m. p. 130—133° raised to 135—136° by a further recrystallisation from butan-1-ol (Found: C, 83·5; H, 6·7. $C_{26}H_{22}O_2,\frac{1}{2}C_4H_9{\cdot}OH$ requires C, 83·35; H, 6·75%), $\lambda_{max.}$ 2550, 2810, and 3110 Å (ε 25,700, 39,200, and 28,400 respectively) in ethanol.

trans-trans-o-*Phenylenedi*-(m-*vinylideneacetoacetylbenzene*) (XIe).—A mixture of the bis-(methyl ketone) (XId) (4·18 g.), sodium ethoxide (from sodium, 1·05 g.), dry ethyl acetate (250 ml.), and dry benzene (150 ml.) was stirred and refluxed for 18 hr. The solid was filtered off and shaken with chloroform (50 ml.) and 0·2N-hydrochloric acid (50 ml.). The organic layer was washed with water (3 × 50 ml.), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was recrystallised once from butan-1-ol, to give the *bis(methyl 1,3-diketone)* (1·90 g., 38%), m. p. 126—128°, raised to 129—130° by a further recrystallisation from butanol (Found: C, 78·5; H, 6·0. $C_{30}H_{26}O_4,\frac{1}{2}BuOH$ requires C, 78·8; H, 6·4%). The compound formed a green *copper chelate* which crystallised from chlorobenzene as plates, m. p. >340° (Found: C, 70·2; H, 4·8; Cu, 12·2%; *M*, 494. $C_{30}H_{24}CuO_4$ requires C, 70·4; H, 4·7; Cu, 12·4%; *M*, 512).

Addition of the bis(methyl 1,3-diketone) (560 mg.) in benzene (10 ml.) and dioxan (10 ml.) to a boiling suspension of magnesium (150 mg.) in dry ethanol (5 ml.) gave the *magnesium chelate* (566 mg., 97%) which, crystallised from butan-1-ol, had m. p. 255—258° (decomp.) (Found: C, 70·5; H, 5·7%; *M*, 513. $C_{30}H_{24}MgO_4,2H_2O$ requires C, 70·8; H, 5·5%; *M*, 508).

16,33-*Diacetyl*-16,17,33,34-*tetrahydro*-15,32H-*hexabenzo*[ab, f, jk, pq, v, yz]*cyclotriacontin*-15,17,32,34-*tetraone* (III).—The bis(acid chloride) (XIb) (2·31 g.) in dry benzene (100 ml.) was added to the magnesium chelate (2·81 g.) of the bis(methyl 1,3-diketone) (XIe) in dry dioxan (100 ml.) and dry benzene (4 l.). The mixture was kept at room temperature for 13 days and then the 1,3-diketonic material was isolated and converted into a mixture of copper chelates as described under the preparation of the macrocycle (II). The mixture of chelates in chloroform (400 ml.) was chromatographed on acid-washed silica gel (500 g.), and the main band was eluted with chloroform to give a solid. The latter was washed with hot benzene (100 ml.) and boiling chlorobenzene (10 ml.) to leave the *copper chelate* (1·18 g., 25%) of the macrocycle (III) as a grey powder, m. p. >340° (Found: C, 76·2; H, 4·7; Cu, 7·5%. $C_{54}H_{36}CuO_6$ requires C, 76·6; H, 4·5; Cu, 7·5%. Treatment of the chelate (1·04 g.) in chloroform (50 ml.) with 5N-hydrochloric acid (50 ml.) at 0° afforded the *macrocycle* (0·83 g., 86%) which darkened at 190—195° but did not melt (Found: C, 82·8; H, 5·2%; *M*, 803. $C_{54}H_{40}O_6$ requires C, 82·6; H, 5·1%; *M*, 785).

o-*Di*-(5-*phenyl*-3,5-*dioxopentyl*)*benzene* (XIVa).—Finely powdered benzoylacetone (8·1 g., 0·05 mole) was added with stirring to a solution of potassamide (from potassium, 3·9 g., 0·1 mole) in liquid ammonia (150 ml.). After ½ hr., *o*-xylylene dibromide (6·7 g., 0·025 mole) in benzene (50 ml.) was rapidly added. The mixture was stirred for 1½ hr., and then ammonium chloride (5 g.) was added. The ammonia was allowed to evaporate while ether was added periodically to maintain a volume of 150 ml. Water (150 ml.) was added, the mixture was acidified with dilute sulphuric acid, and the organic layer was separated and extracted with 2N-sodium hydroxide (3 × 50 ml.). The yellow aqueous solution and the brown syrup which was deposited were separated, and each was acidified with dilute sulphuric acid and then extracted with ether. The yellow solution thus yielded benzoylacetone (2·5 g.), m. p. 55—57°; the syrup yielded sticky brown crystals which were dissolved in methanol (100 ml.). This methanol solution was heated with charcoal, filtered, and cooled, to give the *bis-(1,3-diketone)* (1·54 g.) as straw-coloured needles, m. p. 95—96° unchanged by a further recrystallisation from methanol (Found: C, 78·65; H, 6·3. $C_{28}H_{26}O_4$ requires C, 78·85; H, 6·15%).

Cupric acetate (0·1 g.) in ethanol (15 ml.) was added to the bis(diketone) (0·2 g.) in ethanol (50 ml.). The precipitate which separated was collected and dissolved in dioxan. Addition of light petroleum gave the greyish-green *copper chelate* (0·15 g.), m. p. 254° (Found: C, 68·75; H, 4·9; Cu, 12·8%; *M*, 490. $C_{28}H_{24}CuO_4$ requires C, 68·9; H, 4·95; Cu, 13·05%; *M*, 488).

m-*Di*-(5-*phenyl*-3,5-*dioxopentyl*)*benzene*.—A similar preparation with *m*-xylylene dibromide (6·7 g.) afforded benzoylacetone (3·56 g.), m. p. 52—56°, and the *bis-(1,3-diketone)* (XIVb) (1·65 g.), m. p. 85—86° (Found: C, 78·9; H, 5·9%). When treated with cupric acetate as described above, the bis(diketone) (0·2 g.) formed a *copper chelate* (0·1 g.), m. p. 287° (Found: C, 69·1; H, 4·85; Cu, 12·9%; *M*, 492).

p-*Di*-(5-*phenyl*-3,5-*dioxopentyl*)*benzene*.—Under the same conditions, *p*-xylylene dibromide

(6·7 g.) yielded the *bis*-(1,3-*diketone*) (XIVc) (2·3 g.), m. p. 123—127°, raised to 128—129° by two recrystallisations from methanol (Found: C, 78·7; H, 6·1%). Benzoylacetone (2·4 g.), m. p. 55—57°, was recovered. The precipitate obtained by treatment of the bis(diketone) (0·2 g.) with cupric acetate, as described above, was only partly soluble in dioxan. Addition of light petroleum to the solution afforded the greyish-green *copper chelate* (15 mg.), m. p. 305°, of the diketone (XIVc) (Found: C, 68·7; H, 5·3; Cu, 13·2%).

We thank Professor J. F. Danielli, F.R.S., for suggesting this problem in connection with the toxicity of strontium-90. We are greatly indebted to Dr. L. N. Owen for his sustained help and encouragement. We also express our appreciation to other members of this Department for helpful discussions, and to the Medical Research Council for grants.

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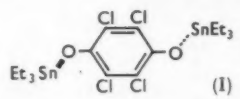
988. *The Crystal and Molecular Structure of Tetrachloro-1,4-bistriethylstannyloxybenzene.*

By P. J. WHEATLEY.

The crystal structure of tetrachloro-1,4-bistriethylstannyloxybenzene has been determined by *X*-ray diffraction methods. The molecules exist in the *trans*-conformation. The Sn–O distance is 2·08 Å.

DURING an investigation of some organotin compounds, we wished to know the conformation of tetrachloro-1,4-bistriethylstannyloxybenzene (I). Models show that free rotation round the C–O bonds is precluded by the bulky chlorine and ethyl groups. The molecules must therefore, be constrained to the *cis*- or *trans*-form. A two-dimensional *X*-ray crystal analysis was carried out to ascertain the molecular geometry, also to determine a value for the Sn–O covalent distance, a value not hitherto recorded.



(I)

Experimental.—$C_{18}H_{30}Cl_4O_2Sn_2$. $M = 657·6$. Monoclinic. $a = 8·72 \pm 0·02$, $b = 11·59 \pm 0·03$, $c = 12·96 \pm 0·03$ Å, $\beta = 97·9° \pm 0·2°$. $U = 1297$ Å^3. $D_m = 1·64$ (by flotation), $Z = 2$, $D_c = 1·683$, $F(000) = 576$. Space group, $P2_1/n$ (C_{2h}^5, No. 14). Cu-K_α radiation ($\lambda = 1·542$ Å), single crystal rotation and Weissenberg photographs.

Multiple-film Weissenberg photographs were taken round [*a*] and [*b*]. Very small crystals were used in order to minimize absorption ($\mu = 197$ cm.$^{-1}$). Relative intensities were estimated visually by comparison with standard strips prepared from the same crystals. 103 0*kl* and 96 *h*0*l* reflexions were observed to be non-zero. Each projection was solved from Patterson syntheses, which served to locate the tin and the chlorine atoms. The lighter atoms were then found from Fourier maps and with the assistance of known lengths and angles. The structure was refined so far as possible by difference syntheses. The final agreement index was $R = 7·5\%$ for the 0*kl* and $R = 7·0\%$ for the *h*0*l* projection. These figures include only the observed reflexions. The scattering factors used were those of Berghuis *et al.*[1] for carbon and oxygen, that of Tomiie and Stam [2] for chlorine, and that of Thomas and Umeda [3] for the tin atom. Thomas and Umeda's figures were corrected for the real part of the dispersion by means of the Table given by Dauben and Templeton.[4] Isotropic temperatures factors $B = 7·9$ Å^2 and 5·7 Å^2 were required for the 0*kl* and *h*0*l* projections, respectively.

[1] Berghuis, Haanappel, Potters, Loopstra, MacGillavry, and Veenendaal, *Acta Cryst.*, 1955, **8**, 478.
[2] Tomiie and Stam, *Acta Cryst.*, 1958, **11**, 126.
[3] Thomas and Umeda, *J. Chem. Phys.*, 1957, **26**, 293.
[4] Dauben and Templeton, *Acta Cryst.*, 1955, **8**, 841.

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TABLE 1.

Fractional co-ordinates.

Atom	*x/a*	*y/b*	*z/c*	Atom	*x/a*	*y/b*	*z/c*	Atom	*x/a*	*y/b*	*z/c*
Sn	0·118	0·767	0·2675	C_1	0·157	0·000	0·028	C_6	0·368	0·755	0·283
Cl_1	0·345	0·988	0·082	C_2	0·060	0·962	0·110	C_7	0·442	0·857	0·350
Cl_2	0·757	0·924	0·146	C_3	0·890	0·962	0·067	C_8	0·978	0·643	0·165
O	0·100	0·933	0·207	C_4	0·032	0·728	0·411	C_9	0·803	0·617	0·167
				C_5	0·942	0·833	0·445				

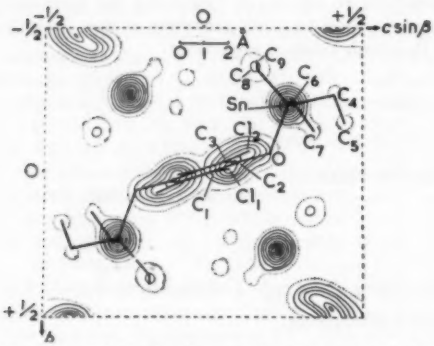

FIG. 1. (a) Projection of the contents of the unit cell down [*a*].

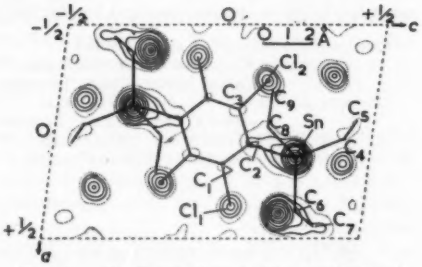

FIG. 1. (b) Projection of the contents of the unit cell down [*b*].

(The contours are drawn at equal, arbitrary intervals, except in the tin peaks, where alternate contours are omitted.)

TABLE 2.

Observed and calculated structure factors for one asymmetric unit.

0*k*l	F_o	F_c	0*k*l	F_o	F_c	0*k*l	F_o	F_c	0*k*l	F_o	F_c	0*k*l	F_o	F_c
0,0,2	42·7	−42·0	3	15·6	−16·4	3	11·1	−11·7	7	2·9	2·4	10	3·6	−2·3
4	12·2	13·3	4	21·4	22·9	4	5·0	6·2	9	2·3	−1·3	12	9·0	8·0
6	22·0	−20·8				5	3·3	2·8	13	3·1	3·4	14	7·0	−7·3
8	6·7	6·4	0,4,5	10·4	11·6	6	4·9	−5·4				16	2·4	2·3
10	5·4	−5·6	6	24·5	−23·6	7	3·4	−3·4	4,0,2	11·5	12·2			
			7	3·6	−3·2				4	26·8	−27·5	3̄,0,1	48·1	49·8
0,1,1	28·0	29·4	8	5·2	5·2	0,8,3	1·2	1·2	6	20·2	22·1	3	32·3	−30·7
2	4·9	5·4	9	2·1	2·1	9	2·4	3·0	10	3·0	2·4	5	8·5	7·3
3	2·6	−2·4							12	1·6	−1·1	7	21·0	−22·5
4	7·5	−6·2	0,5,1	4·8	6·0	0,9,3	4·1	4·6				9	15·4	15·2
5	8·9	−9·8	2	4·4	−5·2	4	4·6	−4·7	5,0,1	17·2	18·4	11	4·9	−5·3
6	17·8	17·7	3	8·5	8·1	5	4·1	−4·4	3	9·6	−10·3	13	4·0	4·8
7	2·4	−3·0	4	9·9	−10·3	7	1·4	1·4	5	12·6	14·0			
8	13·4	−14·7	5	10·2	−9·2	9	2·7	−2·2	7	6·2	−5·2	4̄,0,2	32·5	32·8
10	8·4	8·4	6	10·5	9·1							4	28·5	−28·9
12	5·4	−4·5	7	1·2	0·5	0,11,5	2·1	1·8	5,0,9	6·2	5·9	6	20·3	21·3
14	2·7	2·2	8	6·4	−7·1	7	1·9	−1·0	11	4·9	−5·8	8	4·9	−4·0
			9	3·8	−3·4				13	2·5	2·1			
0,2,0	15·6	−16·1	10	4·9	4·4	*h*0*l*						5̄,0,1	18·3	−18·4
1	21·2	−22·8	11	3·6	4·1	0,0,2	42·1	−42·6	6,0,6	5·9	−6·0	3	2·7	−1·2
2	47·2	47·1	12	1·5	−1·8	4	12·2	14·0	8	4·2	2·8	13	4·7	4·0
3	1·5	−0·8				6	25·0	−25·4	12	2·4	3·3	15	3·5	−4·2
4	36·7	−37·7	0,6,0	16·2	−17·1	8	9·2	7·9						
5	5·7	−4·2	1	19·5	−19·3	10	6·9	−7·9	7,0,3	8·6	−9·1	5̄,0,2	12·2	11·3
6	13·8	14·7	2	22·9	24·6				5	6·4	7·1	6	5·2	5·1
7	3·0	3·4	3	7·4	7·6	1,0,1	32·1	−30·5						
8	10·2	−9·9	4	11·0	−11·1	3	19·1	17·8	8,0,2	5·8	−6·9	5̄,0,3	12·3	−11·9
10	4·4	3·8	5	6·7	−7·1	5	34·3	−32·7	4	5·6	6·5	10	7·6	8·5
			6	3·7	3·8	7	29·2	30·3	6	3·2	−3·7	12	3·4	−3·1
0,3,1	30·0	29·3	7	3·5	3·9	9	7·9	−7·3						
2	32·5	−33·5	8	5·1	−6·1	11	5·2	4·1	9,0,5	4·1	−4·8	7̄,0,1	11·1	−11·7
3	9·6	−8·9	10	2·7	2·3	13	5·9	−6·4				3	20·0	19·6
4	16·2	17·2							1̄,0,1	33·1	30·1	5	9·3	−8·2
6	10·3	−11·7	0,7,1	1·5	−0·5	2,0,2	10·9	11·9	3	32·9	−31·3	7	7·7	6·8
7	7·0	−6·6	2	5·8	−5·1	4	5·5	3·9	5	32·7	33·7	9	3·7	−4·7
8	9·2	10·1	5	2·0	1·9	6	4·7	3·8	9	10·5	−10·4			
9	1·5	0·5	6	4·1	−4·8	8	16·9	−15·3	11	5·4	5·7	5̄,0,2	9·3	−9·7
10	7·6	−6·5	7	6·0	−7·1	10	6·8	5·8	13	3·7	−3·4	6	3·8	−3·3
11	1·9	−1·2	8	6·4	6·3	12	6·9	−7·2	15	2·9	2·9	8	3·9	4·7
12	4·4	4·9	9	3·8	3·8	14	3·4	3·7						
									2̄,0,2	14·3	−15·5	5̄,0,9	3·8	−3·8
0,4,0	36·3	37·3	0,8,0	9·4	9·9	3,0,1	41·5	−42·3	4	9·4	8·5			
1	1·7	−1·5	1	10·4	8·7	3	14·3	13·3	6	17·4	−17·5	1̄0,0,2	3·0	− 4·0
2	18·3	−16·4	2	5·2	−5·6	5	7·4	−6·4	8	14·9	15·1	4	4·1	4·4

Results.—The co-ordinates of the atoms are given in Table 1. Figs. 1a and b show the final Fourier maps for the 0*kl* and *h*0*l* projections respectively. Fig. 2 shows the bond lengths and the numbering of the atoms. The C–Cl bonds are estimated to be accurate to ±0·05 Å, the Sn–O and Sn–C bonds to ±0·06 Å, and the bonds between light atoms to ±0·1 Å. Table 2 gives the observed and the calculated structure factors.

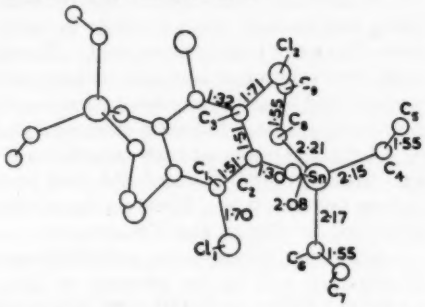

FIG. 2. The numbering of the atoms, and the bond lengths.

The molecules possess centres of symmetry and thus all exist in the *trans*-form in the crystal. No detectable changes were found in the angles formed by the tin atom, which were assumed to be tetrahedral. The plane containing the atoms, Sn, O, and C_2 is normal to the plane of the quinone ring. The Sn–O distance is 2·08 Å, close to the sum of Pauling's covalent radii.[5] The angle at the oxygen is 127°. Other bond lengths, bond angles, and intermolecular distances have normal values.

I thank Dr. G. Weissenberger of this laboratory for the sample.

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[*Received, June 12th,* 1961.]

[5] Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, 1960, p. 164.

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989. *Polycyclic Cinnoline Derivatives. Part IX.*[1] *The Bromination of Benzo[c]cinnoline and the Preparation and Ultraviolet Absorption Spectra of Reference Compounds.*

By J. F. CORBETT and P. F. HOLT.

The electrophilic bromination of benzo[*c*]cinnoline gives 1-bromobenzo[*c*]-cinnoline and the 1,4- or 1,7-dibromo-compound. The preparation of reference compounds involved the use of three routes to benzo[*c*]cinnoline derivatives; three of the four possible bromobenzo[*c*]cinnolines are described, together with some polybromo-derivatives. Lithium aluminium hydride removes bromine atoms from the 1- and the 4-position of benzo[*c*]cinnoline. Bromine atoms in the 4-position prevent *N*-oxidation in the 5(*peri*)-position.

The ultraviolet absorption spectra of the bromobenzo[*c*]cinnolines are recorded. The spectral shifts resulting from the introduction of bromine atoms into benzo[*c*]cinnoline are additive and depend on the position of substitution. Spectra thus provide support for the structure assigned, on chemical evidence, to the dibromo-compound.

DEWAR and MAITLIS [2] calculated the order of reactivity of the four positions of benzo[*c*]-cinnoline (I) towards electrophilic substitution, to be 1 > 3 > 4 > 2. Smith and Ruby [3] showed that nitration of benzo[*c*]cinnoline gave the 1-isomer as the major product and

[1] Part VIII, Corbett and Holt, *J.*, 1961, 3695.
[2] Dewar and Maitlis, *J.*, 1957, 2521.
[3] Smith and Ruby, *J. Amer. Chem. Soc.*, 1954, **76**, 5807.

suggested that the minor product was the 3-isomer. We find that the minor isomer is in fact 4-nitrobenzo[*c*]cinnoline.[4] The bromination of benzo[*c*]cinnoline has therefore been studied in order to compare the results with those of nitration.*

There appears to be no report in the literature of the successful bromination of benzo[*c*]cinnoline (I). Ruby used molecular bromine in a variety of solvents, but obtained no bromobenzo[*c*]cinnoline.[5] We confirmed this, an orange-red solid, $C_{12}H_8Br_{1\cdot5-1\cdot7}N_2$, being precipitated when bromine is added to a solution of benzo[*c*]cinnoline in carbon tetrachloride or boiling acetic acid. The solid is stable at room temperature, but resinifies, with the evolution of bromine, at temperatures above 75°. With acetone it gives bromoacetone and benzo[*c*]cinnoline hydrobromide hydrate, and it liberates iodine from aqueous potassium iodide. Iodine in carbon tetrachloride similarly gives a substance $C_{12}H_8I_{1\cdot7}N_2$.

Cheorvas [6] obtained from cinnoline a bromo-compound with similar properties to ours, and Stoermer and Fincke [7] obtained another from 4-phenylcinnoline with bromine in carbon tetrachloride. These products are probably charge-transfer complexes of the type described by Slough and Ubbelohde.[8]

de la Mare, Kiamud-din, and Ridd brominated quinoline in the *Bz*-ring, using bromine in sulphuric acid in the presence of silver sulphate,[9] the active agent being $BrH_2SO_4^+$ or $BrSO_3^+$,[9] Br^+, or $BrOH_2^+$.[10] Bromination of benzo[*c*]cinnoline by this method gave 27% of a monobromo- and 4% of a dibromo-derivative.

There were no reference compounds with which to compare these products. The establishment of their structure by degradation was not attempted, since the reduction of benzo[*c*]cinnoline normally stops at the *NN'*-dihydro-derivative.[11] Scission of the N–N bond has been achieved by catalytic reduction at high pressure,[12] but under such conditions it seemed likely that the bromine atoms would also be reduced. The identity of the monobromo-derivative was established by synthesising three of the four possible bromobenzo[*c*]cinnolines; 1-bromobenzo[*c*]cinnoline was identical with the reaction product.

Determination of the structure of the dibromo-compound by synthesis would have been tedious since there are fourteen isomers and the ten unsymmetrical compounds would have been particularly difficult to prepare. Evidence establishing its structure as 1,7(or 4)-dibromobenzo[*c*]cinnoline was obtained by synthesis of some reference compounds, which eliminated certain isomers, from a consideration of steric hindrance to *N*-oxidation, from a study of the debromination of bromobenzo[*c*]cinnolines by lithium aluminium hydride, and from ultraviolet absorption spectra.

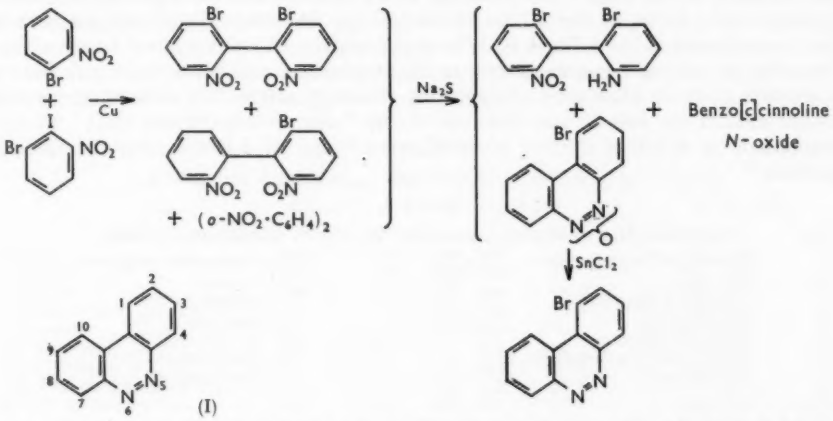
Reduction of the corresponding dinitrobiaryl appeared to be the only route to 1-bromobenzo[*c*]cinnoline. 2-Bromo-6,2'-dinitrobiphenyl can only be formed by a mixed Ullmann reaction from *o*-bromonitrobenzene but the necessary 3-bromo-2-halogenonitrobenzenes are difficult to prepare.[13] A route to 1-bromo-3-methylbenzo[*c*]cinnoline was therefore first worked out starting from the more readily available 3-bromo-4-halogeno-5-nitrotoluenes. 3,4-Dibromo-5-nitrotoluene gave a biphenylene derivative,[14] but the iodo-compound gave mainly 2,2'-dibromo-4,4'-dimethyl-6,6'-dinitrobiphenyl. This compound was

* The failure of molecular-orbital theory to predict the correct orientation for both the nitration and bromination of benzo[*c*]cinnoline will be discussed in a forthcoming paper on the nitration.

[4] Booker, Corbett, and Holt, unpublished work.
[5] Ruby, Ph.D. Thesis, University of Iowa, 1953.
[6] Cheorvas, Thesis, University of California, 1948.
[7] Stöermer and Fincke, *Ber.*, 1909, **42**, 3115.
[8] Slough and Ubbelohde, *J.*, 1957, 918.
[9] de la Mare, Kiamud-din, and Ridd, *J.*, 1960, 561.
[10] Derbyshire and Waters, *J.*, 1950, 572.
[11] Tauber, *Ber.*, 1891, **24**, 197; Wittig and Stichnoth, *Ber.*, 1935, **68***B*, 928; Hata, Tatematsu, and Kubota, *Bull. Chem. Soc. Japan*, 1935, **10**, 425; Kuhn and Erlenmeyer, *Helv. Chim. Acta*, 1955, **38**, 531; Duval, *Bull. Soc. chim. France*, 1910, **7**, 485; Bohlmann, *Chem. Ber.*, 1952, **85**, 390.
[12] Moore and Furst, *J. Amer. Chem. Soc.*, 1957, **79**, 5492; *J. Org. Chem.*, 1958, **23**, 1504.
[13] Körner and Contradi, *Atti R. Acad. Lincei*, 1908, [5], **17**, I, 466.
[14] Corbett and Holt, *J.*, 1961, 4161.

debrominated by lithium aluminium hydride, giving 3,8-dimethylbenzo[*c*]cinnoline, but with sodium sulphide it gave 6-amino-2,2′-dibromo-4,4′-dimethyl-6′-nitrobiphenyl. Although the latter product did not cyclise when refluxed with methanolic sodium hydroxide, cyclisation evidently being hindered by the bulky bromine atoms, a single bromine atom was considered unlikely to inhibit cyclisation.

From these experiments the indicated route to 1-bromobenzo[*c*]cinnoline *N*-oxide was a mixed Ullmann reaction with *o*-bromonitrobenzene and 1-bromo-2-iodo-3-nitrobenzene and reduction of the resulting 2-bromo-6,2′-dinitrobiphenyl with sodium sulphide. The mixed reduction products, rather than the dinitrobiaryls themselves, were separated; the amino-compound was removed by extraction with acid and the sparingly soluble bromobenzo[*c*]cinnoline *N*-oxide was separated from benzo[*c*]cinnoline *N*-oxide by crystallisation from ethanol. The scheme was satisfactory for the preparation of both 1-bromo-3-methylbenzo[*c*]cinnoline *N*-oxide and 1-bromobenzo[*c*]cinnoline *N*-oxide. Reduction of 1-bromo-3-methylbenzo[*c*]cinnoline *N*-oxide with lithium aluminium hydride gave 3-methylbenzo[*c*]cinnoline, but with stannous chloride the bromine was retained. 1-Bromobenzo[*c*]cinnoline *N*-oxide with stannous chloride gave 1-bromobenzo[*c*]cinnoline.



(I)

2-Bromobenzo[*c*]cinnoline 6-oxide was prepared by cyclising 2-amino-5-bromo-2′-nitrobiphenyl. 2,2′-Dinitrobiphenyl was reduced to 2-amino-2′-nitrobiphenyl, the acetyl derivative of which was brominated to give 2-acetamido-5-bromo-2′-nitrobiphenyl. The identity of the latter was proved by its reductive acetylation and subsequent bromination to 2,2′-bisacetamido-5,5′-dibromobiphenyl, previously prepared by Le Fèvre.[15] The acetyl derivative was hydrolysed to the amine which in refluxing methanolic sodium hydroxide gave an almost quantitative yield of 2-bromobenzo[*c*]cinnoline *N*-oxide. This gave 2-bromobenzo[*c*]cinnoline with lithium aluminium hydride.

Oxidation of 2-bromobenzo[*c*]cinnoline with hydrogen peroxide in acetic acid gave the 5- and the 6-oxides, separable by crystallisation.

3-Bromobenzo[*c*]cinnoline was isolated from the mixture obtained by reducing with lithium aluminium hydride the products of a mixed Ullmann reaction between *o*-bromonitrobenzene and 2,5-dibromonitrobenzene. Benzo[*c*]cinnoline was removed with acid; fractional crystallisation of the residue gave 3-bromobenzo[*c*]cinnoline and 3,8-dibromobenzo[*c*]cinnoline. The last compound was also obtained by reducing 4,4′-dibromo-2,2′-dinitrobiphenyl from 2,5-dibromonitrobenzene with lithium aluminium hydride.

Attempts to prepare 4-bromobenzo[*c*]cinnoline from 4-aminobenzo[*c*]cinnoline [4] by a Sandmeyer reaction were unsuccessful.

[15] Le Fèvre, *J.*, 1929, 736.

2,4-Dibromobenzo[*c*]cinnoline was obtained by a method similar to that used for the preparation of the 2-bromo-compound. Bromination of 2-amino-2-nitrobiphenyl gave a dibromo-derivative which on reduction and subsequent bromination gave 3,5,3′,5′-tetrabromo-2,2′-diaminobiphenyl, identical with a specimen formed by the bromination of 2,2′-diaminobiphenyl.[16] The dibromo-compound, which was also obtained by the bromination of 2-amino-5-bromo-2′-nitrobiphenyl, must therefore be 2-amino-3,5-dibromo-2′-nitrobiphenyl. The dibromo-compound, when refluxed with methanolic sodium hydroxide, gave 2,4-dibromobenzo[*c*]cinnoline 6-oxide and this was reduced by stannous chloride to 2,4-dibromobenzo[*c*]cinnoline.

Bromination of 2,2′-diamino-5,5′-dimethylbiphenyl gave its 3,3′-dibromo-derivative which, on oxidation with hydrogen peroxide in acetic acid, gave a quantitative yield of 4,7-dibromo-2,9-dimethylbenzo[*c*]cinnoline.

Structure of the Dibromo-compound obtained by Bromination of Benzo[c]*cinnoline.*—Lithium aluminium hydride removed both bromine atoms from the dibromobenzo[*c*]-cinnoline. To determine from which positions bromine atoms are likely to be abstracted, a number of bromobenzo[*c*]cinnolines were treated with lithium aluminium hydride. The results, given in Table 1, show that bromine atoms in the 1- and the 4-position are always eliminated while those in the 2- and the 3-position are retained and suggest that the dibromo-compound is the 1,10-, 1,4-, 1,7-, or 4,7-isomer. Substitution of 1-bromobenzo-[*c*]cinnoline by a second bromine atom, in the 10-position can, however, be ruled out on the grounds of steric hindrance. Supporting this supposition, the absorption spectrum does not exhibit the loss of fine structure or the " steric bathochromic shift " which is characteristic of 4,5-disubstituted phenanthrenes[17] and of 1,10-disubstituted benzo[*c*]-cinnolines.[18]

TABLE 1.

Debromination of benzo[*c*]cinnolines by lithium aluminium hydride.

Starting benzo[*c*]cinnoline	Benzo[*c*]cinnoline produced
1-Bromo-	Unsubst.
1-Bromo-3-methyl-	3-Methyl-
2,4-Dibromo-	2-Bromo-
2,4,7,9-Tetrabromo-	2,9-Dibromo-
4,7-Dibromo-2,9-dimethyl-	2,9-Dimethyl-
3,8-Dibromo-	(Unchanged)

Oxidation of the dibromo-compound with hydrogen peroxide in acetic acid gave an *N*-oxide. Similar treatment of 1-, 2-, and 3-bromobenzo[*c*]cinnoline resulted in the *N*-oxides, probably mixtures of the 5- and 6-oxides, although both isomers were only isolated in the case of 2-bromobenzo[*c*]cinnoline. Similarly 2,9- and 3,8-dibromobenzo-[*c*]cinnoline gave their *N*-oxides, and 2,4-dibromobenzo[*c*]cinnoline gave its 6-oxide which was identical with that obtained above by the cyclisation of 2-amino-3,5-dibromo-2′-nitrobiphenyl.

No *N*-oxidation occurred when 2,4,7,9-tetrabromobenzo[*c*]cinnoline and 4,7-dibromo-2,9-dimethylbenzo[*c*]cinnoline were treated with hydrogen peroxide in acetic acid. This and the formation of only the 6-oxide from the 2,4-dibromo-compound indicate steric hindrance by the bromine atoms *peri* to the nitrogen atom. It is thus reasonable to suppose that 4,7-dibromobenzo[*c*]cinnoline would also resist *N*-oxidation and that the dibromo-compound obtained by bromination of benzo[*c*]cinnoline is either the 1,4- or the 1,7-isomer, a suggestion which is supported by the ultraviolet absorption spectra.

Of the two possible structures, that of 1,7-dibromobenzo[*c*]cinnoline is preferred;

[16] Corbett and Holt, *J.*, 1961, 3695.

[17] Friedel and Orchin, " Ultra-violet Spectra of Aromatic Compounds," John Wiley & Sons, New York, 1951, p. 23; Friedel, *Appl. Spectroscopy*, 1957, **11**, 13; Johnson, *J. Org. Chem.*, 1959, **24**, 833; Cromartie and Murrell, *J.*, 1961, 2063.

[18] Booker, Corbett, Holt, and Hughes, unpublished work.

XUM

the second bromine atom would probably enter the unsubstituted ring, as the substituted ring would be deactivated by the *—I* effect of the substituent.

The debromination of 1- and 4-bromobenzo[*c*]cinnoline calls for comment since it is unusual for lithium aluminium hydride to reduce aromatic halides. The results do not appear to be explicable in terms of inductive or electromeric effects. Possibly the bromine atom is removed from the 4-position of benzo[*c*]cinnoline during the decomposition of a complex between the cinnoline and aluminium hydride resulting from co-ordination by the lone-pair electrons on the nitrogen atoms. When solutions of benzo[*c*]cinnoline and lithium aluminium hydride in ether are mixed, a green precipitate separates and the yellow colour of the solution disappears. Removal of bromine from the 1-position is possibly due to intramolecular overcrowding which weakens the C–Br bond.

Ultraviolet Absorption Spectra.—The ultraviolet absorption spectrum of benzo[*c*]-cinnoline (I) in non-polar solvents consists of four absorption bands. Three are attributed to π–π^* transitions and have been designated group I (λ *ca.* 250 mμ, log ε *ca.* 4·6), group II (λ *ca.* 300 mμ, log ε *ca.* 3·9), and group III (λ *ca.* 350 mμ, log ε *ca.* 3·2), and each exhibits a certain amount of fine structure.[19] These bands correspond, respectively, to the β-, *p*-, and α-bands (Clar's nomenclature [20]) of phenanthrene. The fourth band is a weak, broad absorption band (λ 400—420 mμ, log ε 2·6) and is attributed to an n–π^* transition.[19]

The spectra of the bromobenzo[*c*]cinnolines were determined to provide further evidence for the structure assigned to the dibromo-compound obtained by the bromination of benzo[*c*]cinnoline. The spectra (Table 2) are similar in form to that of benzo[*c*]cinnoline,

TABLE 2.

Absorption spectra ($\lambda_{max.}$) for some bromobenzo[*c*]cinnolines.

	Group I [a]		Group II [b]		Group III	
Subst.		δλ *		δλ *		δλ *
None	251	0	295, 308	0	331, 347, 362	0
1-Bromo-	251	0	306, 319	11	—, 354, 369	7
2-Bromo-	254	3	302, 314	6·5	331,‘346, 361	−1
2,9-Dibromo-	257	6	308, 320	12·5	—, 345, 360	−2
3-Bromo-	295	8	295, 308	0	340, 355, 371	9
3,9-Dibromo-	266	15	—, 308	0	349, 362, 380	18
2,4-Dibromo-	258	7	311, 325	16·5	—, 352, 368	5·5
2,4,7,9-Tetrabromo-	265	14	331, 343	35·5	—, —, 373	11
1,7(4?)-Dibromo-	254	3	318, 331	23	—, 359, 375	12·5

* Relative to $\lambda_{max.}$ for benzo[*c*]cinnoline. ‘ Shoulder. [a] EtOH as solvent. [b] CCl_4 as solvent.

TABLE 3.

Spectral shifts (mμ) produced by a bromine atom in the various positions in benzo[*c*]cinnoline.

Position	Group I	Group II	Group III
1-	0	11	7
2-	3	6	−1
3-	8	0	9
4-	4	11	6·5

exhibiting a single group I maximum (in ethanol), a group II band having two maxima, and a group III band having three (in carbon tetrachloride), except that, in a number of cases where a large bathochromic shift of one band (relative to that of benzo[*c*]cinnoline) is accompanied by a small shift of the next band, one or more peaks in the latter may be masked or may appear as shoulders.

From Table 2 it can be seen that the shifts produced by the substituents are additive to within 1 mμ, except that the group II shift for the tetrabromo-compound is 2·5 mμ greater than twice the shift for the 2,4-dibromo-compound.

[19] Badger and Walker, *J.*, 1956, 122; Corbett, Holt, and Hughes, *J.*, 1961, 1363.
[20] Clar, " Aromatische Kohlenwasserstoffe," Springer-Verlag, Berlin, 1952.

By estimating the shifts for substitution in the 4-position, on the assumption that the shifts are additive, shifts can be ascribed for substitution by bromine atoms in the four positions of benzo[*c*]cinnoline (Table 3). The spectrum of the 1,7(4?)-dibromo-compound exhibits shifts to be expected for such structures (for the group I, II, and III bands respectively: observed, 3, 23, and 12·5 mμ; estimated 4, 22, and 13·5 mμ).

Experimental

Benzo[c]*cinnoline–Bromine Complexes.*—Bromine was added to a solution of benzo[*c*]-cinnoline [21] in carbon tetrachloride; an orange-red solid separated immediately. The solid was filtered off, washed, and dried in air, at room temperature (Found: C, 47·8; H, 3·0; Br, 40·25; N, 9·3. Calc. for $C_{12}H_8Br_{1\cdot5}N_2$: C, 48·0; H, 2·9; Br, 40·0; N, 9·3%). A similar compound separated as orange-red needles when bromine and benzo[*c*]cinnoline were heated in acetic acid (Found: C, 45·7; H, 2·3; Br, 42·2; N, 9·6. Calc. for $C_{12}H_8Br_{1\cdot66}N_2$: C, 46·0; H, 2·5; Br, 42·5; N, 9·0%.

Recrystallisation of the products from ethanol gave benzo[*c*]cinnoline, m. p. and mixed m. p. 156°, and from acetone gave benzo[*c*]cinnoline hydrobromide hydrate, m. p. 220° [lit.,[22] m. p. 220° (decomp.)].

Benzo[c]*cinnoline–Iodine Complexes.*—Benzo[*c*]cinnoline (0·5 g.) in carbon tetrachloride (5 ml.) was added to a solution of iodine (1·0 g.) in carbon tetrachloride (10 ml.). After 2 hr. at room temperature, the complex was filtered off, washed with a little carbon tetrachloride, and allowed to dry (Found: C, 35·8; H, 2·4; I, 54·9; N, 6·9. Calc. for $C_{12}H_8I_{1\cdot12}N_2$: C, 36·0; H, 2·0; I, 54·9; N, 7·0%).

Bromination of Benzo[c]*cinnoline.*—Benzo[*c*]cinnoline (1·8 g.) in sulphuric acid (5 ml.) was treated with silver sulphate (1·7 g.) and bromine (0·52 ml.) in sulphuric acid (15 ml.). The mixture was shaken for 2 hr. and then filtered. The filtrate was poured into water (500 ml.), and the precipitate was filtered off, washed with water and dried. Basification of the aqueous filtrate gave benzo[*c*]cinnoline (0·75 g., 42%). The mixture of bromo-compounds was a yellow powder, m. p. 140—160° (from ethanol) (0·98 g.). A sample (0·1 g.) was chromatographed on alumina (10 × 0·75 cm.), and the eluate was collected in four fractions: (i) m. p. 146—149°, (ii) m. p. 144—149°, (iii) m. p. 194—199°, (iv) m. p. 197—199°. Recrystallisation of fractions (iii) and (iv) from ethanol gave 1-bromobenzo[*c*]cinnoline (0·06 g.) as bright yellow needles, m. p. 199°; the mixed m. p. with an authentic sample was 198—199° and the absorption spectra of the two samples were identical.

Recrystallisation of fractions (i) and (ii) from benzene gave 1,7(or 4)-*dibromobenzo*[c]*cinnoline* (0·015 g.) as bright yellow needles, m. p. 193° (mixed m. p. with 1-bromobenzo[*c*]cinnoline, 156—160°) (Found: C, 42·6; H, 1·7; Br, 46·5; N, 8·3. $C_{12}H_6Br_2N_2$ requires C, 42·5; H, 1·8; Br, 47·3; N, 8·3%). The mother liquor yielded a further crop of 1-bromobenzo[*c*]cinnoline (0·013 g.).

The remainder of the mixed products was separated qualitatively in a similar fashion.

1,7(or 4)-*Dibromobenzo*[c]*cinnoline* 5(or 6)-*Oxide.*—The dibromocinnoline (20 mg.) in acetic acid (2 ml.) was treated with 80% w/v hydrogen peroxide (0·1 ml.) at 50° for 1 hr. Water was added and the precipitate was filtered off and recrystallised from acetic acid as pale yellow needles, m. p. 241° (Found: C, 40·25; H, 1·7; Br, 45·3; N, 7·9. $C_{12}H_6Br_2N_2O$ requires C, 40·6; H, 1·7; Br, 45·2; N, 7·9%).

Reduction of 6,6′-Dibromo-4,4′-dimethyl-2,2′-dinitrobiphenyl.—With lithium aluminium hydride. The biaryl [14] (2 g.) in dry benzene (150 ml.) and dry ether (100 ml.) was treated with lithium aluminium hydride (1 g.) in ether (75 ml.). The mixture was left at room temperature for 2 hr. and warmed on a water bath for 15 min., then cooled. Water was added to decompose the excess of hydride and the mixture was filtered. The filtrate was evaporated and the residue was chromatographed in benzene on alumina; evaporation of the eluate and recrystallisation of the residue from ethanol gave 3,8-dimethylbenzo[*c*]cinnoline (0·8 g., 80%), m. p. and mixed m. p. 186°.

With sodium sulphide. The biaryl (2 g.) in boiling ethanol (100 ml.) was treated with sodium sulphide nonahydrate (2 g.) and sodium hydroxide (0·1 g.) in water (10 ml.), and the mixture was heated under reflux for 4 hr. The mixture was filtered and the filtrate was evaporated

[21] Badger, Seidler, and Thomson, *J.*, 1951, 3207.
[22] Corbett and Holt, *J.*, 1960, 3646.

to low bulk and poured into water. The precipitate was recrystallised four times from benzene to give *2-amino-6,6′-dibromo-4,4′-dimethyl-2′-nitrobiphenyl* as orange rhombs., m. p. 128° (Found: Br, 42·8; N, 6·7. $C_{14}H_{12}Br_2N_2O_2$ requires Br, 42·9; N, 6·7%).

1-Bromo-3-methylbenzo[c]*cinnoline.—The Ullmann reaction.* 3-Bromo-4-iodo-5-nitrotoluene [14] (12 g.) and *o*-bromonitrobenzene (10 g.) were refluxed with copper bronze (15 g.) in dimethylformamide (150 ml.) for 8 hr. The mixture was allowed to cool, then filtered, and the filtrate was poured into water. The precipitate was filtered off, dried, and extracted with boiling benzene. The extract was evaporated and the residue used for the next stage.

Reduction of the biaryls. The oil obtained as above (7·8 g.) in boiling ethanol (150 ml.) was heated with sodium sulphide nonahydrate (12 g.) and sodium hydroxide (2·5 g.) in water (20 ml.) for 4 hr. The mixture was filtered while hot, evaporated to low bulk, and poured into water. The oil which separated was dissolved in benzene and the solution was extracted with 1 : 1 v/v aqueous hydrochloric acid. The benzene solution was washed with water, dried, and chromatographed on alumina to remove tar. Concentration of the yellow eluate gave, on cooling, *1-bromo-3-methylbenzo*[c]*cinnoline N-oxide* (0·4 g., 4%) as pale yellow needles, m. p. 245° (Found: C, 54·45; H, 3·28; Br, 26·95; N, 9·7. $C_{13}H_9BrN_2O$ requires C, 54·0; H, 3·12; Br, 27·6; N, 9·7%). The mother liquor gave benzo[*c*]cinnoline *N*-oxide, m. p. and mixed m. p. 140°. The acid extract was basified and the precipitate filtered off and recrystallised from benzene, to give 2-amino-6,6′-dibromo-4,4′-dimethyl-2′-nitrobiphenyl, m. p. and mixed m. p. 128°.

Reduction of the N-oxide. (*a*) The *N*-oxide (0·1 g.) was reduced with lithium aluminium hydride (0·1 g.) as above. The product, which was an oil, was dissolved in ethanol and treated with picric acid. *3-Methylbenzo*[c]*cinnoline picrate* separated as yellow needles, m. p. 176° (Found: C, 54·3; H, 3·1. $C_{19}H_{13}N_5O_7$ requires C, 53·9; H, 3·1%). The picrate, in ethanol, was filtered through a column of alumina; evaporation of the eluate gave 3-methylbenzo[*c*]cinnoline, m. p. 98—100°, which was identical with a sample prepared [4] by reduction of 4-methyl-2,2′-dinitrobiphenyl [23] with lithium aluminium hydride.

(*b*) The *N*-oxide (0·1 g.) was suspended in hydrochloric acid (10 ml.), and a solution of stannous chloride (0·2 g.) in hydrochloric acid (10 ml.) was added. The mixture was kept at 80—90° for 3 hr., water was added, and the solid material was filtered off. *1-Bromo-3-methylbenzo*[c]*cinnoline* formed yellow needles (from ethanol) (0·04 g.), m. p. 154° (Found: C, 57·0; H, 3·2; Br, 29·0; N, 10·15. $C_{13}H_9BrN_2$ requires C, 57·1; H, 3·3; Br, 29·2; N, 10·25%).

1-Bromo-2-iodo-3-nitrobenzene.—2-Bromo-6-nitroaniline [13] (10·5 g.) in cold acetic acid (50 ml.) was added, with stirring, to a solution of sodium nitrite (3·8 g.) in sulphuric acid (50 ml.). The resulting solution was poured into an excess of saturated aqueous potassium iodide. After 15 min., water was added and the solid was filtered off, dissolved in ether, and washed with aqueous sodium metabisulphite and water. The ether solution was dried and the ether evaporated. The residue recrystallised from ethanol, to give 1-bromo-2-iodo-3-nitrobenzene (11·8 g., 72%), m. p. 115° (lit., m. p. 119°).

1-Bromobenzo[c]*cinnoline.*—The mixed Ullmann reaction was carried out, as above, with 1-bromo-2-iodo-3-nitrobenzene (11·8 g.) and *o*-bromonitrobenzene (8 g.). The resulting oil was reduced with sodium sulphide, and the products were separated as described above. *1-Bromobenzo*[c]*cinnoline N-oxide* formed pale yellow needles (0·3 g.), m. p. 225—227° (Found: C, 51·7; H, 2·8; Br, 29·3; N, 9·95. $C_{12}H_7BrN_2O$ requires C, 52·4; H, 2·5; Br, 29·1; N, 10·2%).

The *N*-oxide was reduced with stannous chloride, as above, to give *1-bromobenzo*[c]*cinnoline*, m. p. 199° (Found: C, 55·2; H, 2·6; Br, 31·2; N, 10·75. $C_{12}H_7BrN_2$ requires C, 55·6; H, 2·7; Br, 30·9; N, 10·8%).

2-Amino-5-bromo-2′-nitrobiphenyl.—2-Amino-2′-nitrobiphenyl [24] with acetic anhydride gave 2-acetamido-2′-nitrobiphenyl, m. p. 155—157° (lit.,[25] m. p. 159—160°).

The nitro-amide (2·1 g.) in acetic acid (15 ml.) was treated with bromine (0·42 ml.) in acetic acid (10 ml.). The mixture was left at room temperature for 4 hr. and then poured into water. The precipitate was recrystallised from benzene–light petroleum (b. p. 60—80°), to give 2-acetamido-5-bromo-2′-nitrobiphenyl as colourless needles, m. p. 75°. This product, in ethanol, was refluxed with hydrochloric acid for 3 hr. The solution was evaporated to low bulk, then

[23] Baker, Barton, and McOmie, *J.*, 1958, 2661.
[24] Badger and Sasse, *J.*, 1957, 4.
[25] Purdie, *J. Amer. Chem. Soc.*, 1941, **63**, 2276.

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basified, and the precipitate was filtered off and recrystallised from ethanol. **2-*Amino*-5-*bromo*-2′-*nitrobiphenyl*** forms yellow needles, m. p. 133° (Found: C, 48·95; H, 3·19; N, 9·6. $C_{12}H_9BrN_2O_2$ requires C, 49·15; H, 3·07; N, 9·55%).

Reductive Acetylation, and Bromination, of **2-*Acetamido*-5-*bromo*-2′-*nitrobiphenyl*.**—The amide (0·5 g.) in acetic acid (20 ml.) was refluxed with zinc dust (2 g.). After 2 hr., acetic anhydride (1 ml.) was added and refluxing was continued for a further 2 hr. Water was added to decompose any excess of anhydride, and the remaining zinc was filtered off. The filtrate was treated with bromine (0·2 ml.), and the solution was warmed on a water bath for 1 hr., concentrated, and allowed to cool. 2,2′-Bisacetamido-5,5′-dibromobiphenyl (0·3 g.) separated as colourless crystals, m. p. 264° (lit., 266—267°). The mixed m. p. with an authentic sample [15] was 264—266°.

2-*Bromobenzo*[c]*cinnoline* 6-*Oxide*.—2-Amino-5-bromo-2′-nitrobiphenyl (0·7 g.) in N-methanolic sodium hydroxide (50 ml.) was heated under reflux for 1 hr. (pale yellow needles started to separate after 5 min.). The mixture was cooled and the product (0·59 g., 90%) was filtered off. **2-*Bromobenzo*[c]*cinnoline* 6-*oxide*** formed pale yellow needles, m. p. 248° (from ethanol) (Found: C, 52·34; H, 2·63; Br, 29·1; N, 10·16. $C_{12}H_7BrN_2O$ requires C, 52·4; H, 2·54; Br, 29·1; N, 10·2%).

2-*Bromobenzo*[c]*cinnoline*.—The *N*-oxide (0·3 g.) was suspended in benzene (15 ml.) and ether (20 ml.), and lithium aluminium hydride (0·3 g.) in ether (10 ml.) was added. The mixture was refluxed for 0·5 hr. After the solution had cooled, water was added to decompose the excess of hydride, and the mixture was filtered. The filtrate was dried and evaporated, and the residue was recrystallised from benzene, giving **2-*bromobenzo*[c]*cinnoline*** (0·27 g., 93%) as yellow needles, m. p. 220° (Found: C, 55·5; H, 2·66; Br, 30·9; N, 10·7. $C_{12}H_7BrN_2$ requires C, 55·6; H, 2·7; Br, 30·9; N, 10·8%).

Oxidation of **2-*Bromobenzo*[c]*cinnoline*.**—The cinnoline was oxidised with hydrogen peroxide in acetic acid as described above. Fractional crystallisation of the product gave the 6-oxide, m. p. and mixed m. p. 248°, and **2-*bromobenzo*[c]*cinnoline* 5-*oxide***, m. p. 230—232° (mixed m. p. with the 6-oxide 220—222°) (Found: C, 52·4; H, 2·54; Br, 29·1; N, 10·2%).

2-*Amino*-3,5-*dibromo*-2′-*nitrobiphenyl*.—(*i*) 2-Amino-2′-nitrobiphenyl (0·52 g.) in acetic acid (8 ml.) was treated with bromine (0·8 g.) in acetic acid (5 ml.). After 2 hr., water was added and the precipitate was filtered off, dried, and recrystallised from ethanol. **2-*Amino*-3,5-*dibromo*-2′-*nitrobiphenyl*** formed orange-yellow needles, m. p. 117° (0·86 g., 94%) (Found: C, 38·0; H, 2·08; Br, 42·7; N, 7·4. $C_{12}H_8Br_2N_2O_2$ requires C, 38·7; H, 2·15; Br, 42·95; N, 7·55%).

(*ii*) 2-Amino-5-bromo-2′-nitrobiphenyl was brominated as above, giving the 3,5-dibromo-compound, m. p. and mixed m. p. 117°.

Reduction and Bromination of **2-*Amino*-3,5-*dibromo*-2′-*nitrobiphenyl*.**—The nitro-compound (0·2 g.) in acetic acid was refluxed with zinc dust for 3 hr. The excess of zinc was filtered off, and bromine (0·3 g.) was added to the filtrate. After 1 hr. the solution was concentrated and allowed to cool. 2,2′-Diamino-3,5,3′,5′-tetrabromobiphenyl separated as almost colourless crystals, m. p. 170°. The mixed m. p. with an authentic sample [16] was 170°.

2,4-*Dibromobenzo*[c]*cinnoline* 6-*Oxide*.—2-Amino-3,5-dibromo-2′-nitrobiphenyl (0·4 g.) in N-methanolic sodium hydroxide (50 ml.) was heated under reflux for 2 hr. After cooling, the product was filtered off and recrystallised from ethanol. **2,4-*Dibromobenzo*[c]*cinnoline* 6-*oxide*** formed almost colourless needles (0·38 g., 98%), m. p. 273° (Found: C, 40·4; H, 1·61; Br, 45·15; N, 8·0. $C_{12}H_6Br_2N_2O$ requires C, 40·6; H, 1·69; Br, 45·2; N, 7·9%).

A reaction time of 45 min. gave only 60% of the *N*-oxide.

2,4-*Dibromobenzo*[c]*cinnoline*. The *N*-oxide (0·2 g.) was reduced with stannous chloride as above. **2,4-*Dibromobenzo*[c]*cinnoline*** formed yellow needles (from ethanol), m. p. 206° (Found: C, 42·6; H, 1·7; Br, 47·4; N, 8·1. $C_{12}H_6Br_2N_2$ requires C, 42·5; H, 1·8; Br, 47·3; N, 8·3%).

Reduction of the *N*-oxide with lithium aluminium hydride gave 2-bromobenzo[*c*]cinnoline, m. p. and mixed m. p. 220°.

3-*Bromobenzo*[c]*cinnoline*.—*The mixed Ullmann reaction.* 1,4-Dibromo-2-nitrobenzene (7 g.) and *o*-bromonitrobenzene (5 g.) in dimethylformamide (100 ml.) were refluxed with copper bronze (10 g.) for 8 hr. The mixed products were isolated as above.

Reduction of the mixture of biaryls. The mixed biaryls (4 g.) were reduced with lithium aluminium hydride, as above. The products were dissolved in benzene and the solution was

extracted with 5N-sulphuric acid to remove benzo[*c*]cinnoline (1·2 g.), m. p. and mixed m. p. 154°. The benzene solution was evaporated, and the residue was fractionally recrystallised from ethanol to give 3,8-dibromobenzo[*c*]cinnoline, and 3-*bromobenzo*[c]*cinnoline* (0·2 g.) as a pale yellow powder, m. p. 191° (Found: C, 55·2; H, 2·6; Br, 31·1; N, 10·7. $C_{12}H_7BrN_2$ requires C, 55·6; H, 2·7; Br, 30·9; N, 10·8%).

4,4′-Dibromo-2,2′-dinitrobiphenyl.—1,4-Dibromo-2-nitrobenzene (14 g.) in dimethylformamide (100 ml.) was refluxed with copper bronze (8 g.) for 6 hr. The mixture was filtered and the filtrate was poured into water. The precipitate was extracted with ethanol, and the extract was concentrated and allowed to cool. The biaryl (7·6 g., 76%) separated as yellow rhombs, m. p. 150° (lit., m. p. 150°).

3,8-*Dibromobenzo*[c]*cinnoline.*—4,4′-Dibromo-2,2′-dinitrobiphenyl (1·4 g.) was reduced with lithium aluminium hydride as above. 3,8-*Dibromobenzo*[c]*cinnoline* (0·87 g., 72%) formed pale yellow needles, m. p. 237° (Found: C, 43·25; H, 1·78; Br, 46·8; N, 8·2. $C_{12}H_6Br_2N_2$ requires C, 42·5; H, 1·79; Br, 47·3; N, 8·3%).

Oxidation of the cinnoline with hydrogen peroxide, as above, gave 3,8-*dibromobenzo*[c]-*cinnoline N-oxide* as pale yellow needles, m. p. 263° (Found: C, 40·6; H, 1·74; Br, 45·15; N, 7·8. $C_{12}H_6Br_2N_2O$ requires C, 40·6; H, 1·69; Br, 45·2; N, 7·9%).

2,2′-Diamino-3,3′-dibromo-5,5′-dimethylbiphenyl.—2,2′-Diamino-5,5′-dimethylbiphenyl [26] (1·5 g.) in acetic acid (20 ml.) was treated with bromine (2 g.). The product was precipitated by the addition of water, and recrystallised from ethanol as a white powder, m. p. 139—140°. The crude material was chromatographed in benzene on alumina, to give *2,2′-diamino-3,3′-dibromo-5,5′-dimethylbiphenyl* as colourless feathery needles, m. p. 150—152° (Found: C, 45·1; H, 3·9; Br, 43·1; N, 7·4. $C_{14}H_{14}Br_2N_2$ requires C, 45·4; H, 3·8; Br, 43·2; N, 7·6%).

4,7-Dibromo-2,9-dimethylbenzo[c]*cinnoline.*—2,2′-Diamino-3,3′-dibromo-5,5′-dimethylbiphenyl (0·3 g.) in acetic acid (20 ml.) was treated with 80% w/v hydrogen peroxide (1 ml.), and the mixture was heated on a water bath for 1 hr. On cooling of the solution, 4,7-*dibromo-2,9-dimethylbenzo*[c]*cinnoline* (0·26 g., 87%) separated as bright yellow needles, m. p. > 370° (Found: C, 46·2; H, 2·82; Br, 43·3; N, 7·5. $C_{14}H_{10}Br_2N_2$ requires C, 45·9; H, 2·74; Br, 43·7; N, 7·65%).

Debromination of Bromobenzo[c]*cinnolines.*—The cinnoline (0·1 g.) was dissolved in 2 : 1 v/v benzene–ether (25 ml.), and lithium aluminium hydride (0·2 g.) in dry ether (10 ml.) was added. The mixture was refluxed for 1 hr. and then allowed to cool. Water was added to decompose the excess of hydride and the mixture was filtered. The filtrate was dried and evaporated, and the residue was recrystallised from ethanol. The products were identified by mixed m. p.s with authentic samples.

Spectra.—The absorption spectra were determined in carbon tetrachloride (B.D.H. spectroscopic grade), a Unicam S.P. 500 spectrophotometer being used.

The authors are grateful to the Royal Society for the loan of a spectrophotometer.

THE UNIVERSITY, READING. [*Received, June 16th*, 1961.]

[26] Case and Koft, *J. Amer. Chem. Soc.*, 1941, **63**, 510.

NOTES.

990. *The Preparation of* DL-α-*Methylhistidine Dihydrochloride.*

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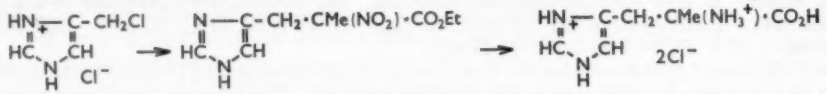
THE three enzymes β-(3,4-dihydroxyphenyl)alanine decarboxylase, 5-hydroxytryptophan decarboxylase, and histidine decarboxylase are all inhibited by DL-β-(3,4-dihydroxyphenyl)-α-methylalanine (α-methyl-DOPA),[1] and 5-hydroxytryptophan decarboxylase is inhibited by 5-hydroxy-α-methyltryptophan (α-methyl-5HTP).[2] As the synthesis of the histidine analogue of the last compound, α-methylhistidine, has not been reported,

[1] Sourkes, *Arch. Biochem.*, 1954, **51**, 444; Smith, *Brit. J. Pharmacol.*, 1960, **15**, 319; Mackay and Shepherd, *ibid.*, p. 552; Udenfriend, Lovenberg, and Weissbach, *Fed. Proc.*, 1960, **19**, 7; Weissbach, Lovenberg, and Udenfriend, *Biochem. Biophys. Res. Comm.*, 1960, **3**, 225.

[2] Heinzelman, Anthony, Lyttle, and Szmuszkovicz, *J. Org. Chem.*, 1960, **25**, 1548.

we have prepared it, for study as a potential inhibitor of the above enzymes, by the route outlined in the formulæ.



The pharmacological studies on α-methylhistidine will be reported elsewhere.

Experimental.—*4-Chloromethylimidazole hydrochloride.* 4-Hydroxymethylimidazole hydrochloride [3] (30 g.) was added in portions of about 5 g. to redistilled thionyl chloride (125 c.c.) with shaking. After the initial exothermic reaction the solution was refluxed for 1 hr., during which time a light brown oil separated and solidified. The excess of thionyl chloride was then evaporated off, and the residual light brown solid recrystallized from ethanol–ether as off-white prisms, m. p. 139—141° (lit.,[4] 138—141°) (32·6 g., 96%).

Ethyl DL-*β-imidazol-4-yl-α-methyl-α-nitropropionate.* To a solution from sodium (4·2 g.) in dry ethanol (75 c.c.) at 0° was rapidly added with stirring a solution of ethyl α-nitropropionate [5] (17·4 g.) in dry ethanol (20 c.c.). An exothermic reaction ensued, and almost immediately the sodium salt of the nitro-ester crystallized. Stirring and cooling were continued, and 4-chloromethylimidazole hydrochloride (8·2 g.) in dry ethanol (100 c.c.) was added in about 30 min. Stirring was continued at room temperature for 36 hr. after which the ethanol was evaporated. The solid residue was dissolved in ice-cold 2N-hydrochloric acid, and extracted with ethyl acetate (3 × 60 c.c.). The aqueous solution was basified with an excess of saturated aqueous sodium carbonate and the base extracted with chloroform (4 × 75 c.c.), dried, and recovered as a light brown gum which crystallized on trituration with ethanol. Recrystallization from ethanol yielded white prisms, m. p. 116—118° (5·15 g., 32·5%). A further crop, m. p. 113—116° (1·6 g., 10%), was obtained by concentration of the mother-liquors. The pure *product* crystallized from ethanol as prisms, m. p. 119—121° (Found: C, 47·7; H, 5·95; N, 18·7. $C_9H_{13}N_3O_4$ requires C, 47·6; H, 5·7; N, 18·5%), $\lambda_{max.}$ 207—209 mμ (ε 7300 in EtOH), $\nu_{max.}$ (in Nujol) 1750s (C=O) and 1560s cm.$^{-1}$ (NO_2).

The ethyl acetate extracts, on drying and evaporation, gave a yellow oil (7·5 g.) that partially solidified under ether (m. p. 149—155°; 0·37 g.). Two recrystallizations from ethanol–ether gave *ethyl* DL-*β-imidazol-4-yl-α-methyl-α-nitropropionate hydrochloride* as needles, m. p. 164—165° (Found: C, 40·9; H, 5·4; N, 15·2, 15·9. $C_9H_{14}ClN_3O_4$ requires C, 41·05; H, 5·3; N, 15·95%), $\lambda_{max.}$ 207—210 mμ (ε 7500 in EtOH), $\nu_{max.}$ (in Nujol) 1760s (C=O), 1560s (NO_2), and 2700b cm.$^{-1}$ (NH^+). The product was readily soluble in water, giving a positive test for chloride. The ether-soluble material was unchanged ethyl α-nitropropionate (6·9 g.).

DL-*α-Amino-β-imidazol-4-yl-α-methylpropionic acid dihydrochloride* (DL-*α-Methylhistidine dihydrochloride*). A solution of ethyl DL-β-imidazol-4-yl-α-methyl-α-nitropropionate (4·0 g.) in ethanol (200 c.c.) was stirred at room temperature with hydrogen at 50 atm. for 14 hr. in the presence of platinum oxide (1 g.). Removal of the platinum and evaporation gave an oil (3·4 g., 96·5%) which did not crystallize and had $\lambda_{max.}$ 210—211 mμ (in EtOH), $\nu_{max.}$ (liquid film) 1740s (C=O), 3200bs cm.$^{-1}$ (NH) but no band at 1560 cm.$^{-1}$ (NO_2 absent).

The crude amine was heated in 11N-hydrochloric acid (25 c.c.) on a steam bath for 30 hr., and the solution was evaporated. The resulting brown gum (4·2 g.) crystallized from warm ethanol on addition of an equal volume of 11N-hydrochloric acid, to give white prisms, m. p. 183—185° (3·62 g., 87%). Recrystallization from ethanol–11N-hydrochloric acid gave pure DL-*α-methylhistidine dihydrochloride* as cubes, m. p. 184—185° (Found: C, 34·95; H, 5·65; N, 16·4. $C_7H_{13}Cl_2N_3O_2$ requires C, 34·85; H, 5·4; N, 17·4%), $\lambda_{max.}$ 211 mμ (ε 4820 in EtOH) [cf. histidine hydrochloride, $\lambda_{max.}$ 210—211 mμ (ε 4200 in EtOH)], $\nu_{max.}$ (in Nujol) 1725s (C=O) and 2500sb cm.$^{-1}$ (NH^+), pK_a 2·4 ± 0·1, 6·1 ± 0·1, and 9·9 ± 0·1 (cf. histidine dihydrochloride, pK_a 2·35 ± 0·1, 6·1 ± 0·1, and 9·6 ± 0·1).

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[3] Totter and Darby, *Org. Synth.*, 1944, **24**, 64.
[4] Turner, Huebner, and Scholz, *J. Amer. Chem. Soc.*, 1949, **71**, 2801.
[5] Kornblum and Blackwood, *Org. Synth.*, 1957, **37**, 44.

991. *Spectra of Ruthenates and Perruthenates.*

By J. L. Woodhead and J. M. Fletcher.

Ultraviolet Spectra.—A much used method [1] for determining ruthenium is based on its oxidation to ruthenate and measurement of the optical densities of the solution in the ultraviolet region. There are, however, conflicting values [1,2,3] for the molar extinction coefficients (ε_{Ru}) of ruthenate and perruthenate ions. We have redetermined these coefficients and at the same time have found the estimation of ruthenium in many of its complexes to be simpler and more reliable when the solution is converted with persulphate into a mixture, in any proportions over a wide range, of ruthenate and perruthenate and the value of ε_{Ru} at the isosbestic point is used.[3]

Primary standards used previously have been (*a*) the metal, (*b*) salts in which the ruthenium has been estimated by reduction to metal, and (*c*) ruthenium tetroxide. With (*a*) and (*b*) as standards, we find for various ruthenate–perruthenate mixtures in 2M-potassium hydroxide at 21°, an isosbestic point at 415 mμ with ε_{Ru} 1047, 1053, 1055 for solutions from the metal; with ε_{Ru} 1044, 1038 for those from commercial ruthenium trichloride; and with ε_{Ru} 1058, 1046 for those from $[RuNO{\cdot}OH(NH_3)_4]Cl_2$. There is a second isosbestic point at 273 mμ for which ε_{Ru} is 1005.

Determinations for ε_{Ru} at 460 mμ ($\lambda_{max.}$ for ruthenate) and at 385 mμ ($\lambda_{max.}$ for perruthenate) gave:

For ruthenate solutions	at 460 mμ	1714,	1720,	1700,	1715,	1716,	1692,	1720
	at 385 mμ	820,	830,	825,	826,	815,	865,	840
For perruthenate solutions ...	at 460 mμ	269,	290,	310,	256,	264		
	at 385 mμ	2170,	2176,	2183,	2162,	2175		

There was no significant difference between measurements at 15° and 30°. Averages of the figures are given in Table 1 along with previous determinations.

Table 1.

Values of ε_{Ru} in KOH solutions.

	Temp.	Ruthenate			Perruthenate			*X*
Wavelength (mμ)		317	385	460	317	385	460	
Marshall and Rickard [1] ...	25°	—		1742	—	—	—	—
Connick and Hurley [2]	25	~500	1030	1820	~2500	2275	283	1·23
Woodhead [3]	21	—	886	1692	—	2162	269	1·04
Larsen and Ross [3a]	—	—	—	1730	—	2150	—	—
This work	21	301	831	1710	2302	2173	278	1·06

A suitable criterion to apply to these and the earlier results is the value they give for the ratio *X*, defined as $(\varepsilon_{ruthenate} - \varepsilon_{perruthenate})_{460\ m\mu}/(\varepsilon_{perruthenate} - \varepsilon_{ruthenate})_{385\ m\mu}$. It can be shown that *X* is also equal to $\Delta D_{460\ m\mu}/\Delta D_{385\ m\mu}$ where ΔD is the change in optical density of a particular solution, identical except for a difference in the ratio of ruthenate to perruthenate. Alkaline solutions of potassium perruthenate are convenient for the determination of *X* because the conversion into ruthenate, $RuO_4^- + OH^- \longrightarrow >RuO_4^{2-}$, is slow at room temperature. Changes in the optical densities, measured in 1 cm. cells, of a solution of $3{\cdot}22 \times 10^{-4}$M-potassium perruthenate in M-potassium hydroxide at successive times after dissolution are given in Table 2.

The constancy of *D* at the isosbestic points 273 and 415 mμ showed that species other than ruthenate and perruthenate were not absorbing. The average of the values for *X*, 1·06, so found, when compared (Table 1) with those calculated from the reported values

[1] Marshall and Rickard, *Analyt. Chem.*, 1950, **22**, 745.
[2] Connick and Hurley, *J. Amer. Chem. Soc.*, 1952, **74**, 5012.
[3] Woodhead, U.K.A.E.A. Document, A.E.R.E.—R 3279, 1960.
[3a] Larsen and Ross, *Analyt. Chem.*, 1959, **31**, 176.

for ε_{Ru} at 385 and 460 mμ, supports the correctness of the figures now presented. For the same perruthenate solution, the optical densities at 317 mμ (where perruthenate shows a second peak) were also measured and the ratio $(\varepsilon_{ruthenate} - \varepsilon_{perruthenate})_{460\ m\mu}/(\varepsilon_{perruthenate} - \varepsilon_{ruthenate})_{317\ m\mu}$ was found to be 1·42. This ratio, in conjunction with a measured value of ε_{Ru} for ruthenate at 317 mμ, was used to obtain ε_{Ru} for perruthenate (Table 1) at this wavelength. This was necessary because the persulphate, added in the procedure to ensure freedom from ruthenate, absorbs strongly at 317 mμ.

TABLE 2.

Time (min.)	10	32	55	80
$\Delta D_{460\ m\mu}$	+0·42	+0·92	+1·68	+2·57
$\Delta D_{385\ m\mu}$	−0·39	−0·87	−1·61	−2·42
$\Delta D_{460\ m\mu}/D_{385\ m\mu}$ (= X)	1·07	1·06	1·04	1·06

The rather high values (Table 1) of Connick and Hurley may arise from their employing molar extinction coefficients for ruthenium tetroxide which are high; values lower by 5% have been given for these coefficients.[4]

Infrared Spectrum (with A. M. DEANE).—Apart from a weak band (overtone or combination) at 1656 cm.$^{-1}$, potassium perruthenate showed only a very strong broad band, partly resolved, at 827 and 846 cm.$^{-1}$. The occurrence of this metal–oxygen stretching band at a frequency lower than for $[MnO_4]^-$ (900 cm.$^{-1}$) and for $[ReO_4]^-$ (913 cm.$^{-1}$) implies that the range, 900—1100 cm.$^{-1}$, proposed [5] for the diagnosis of M=O bonds, should be extended to lower frequencies, since the bond length, 1·79 Å, for Ru=O in $[RuO_4]^-$ is consistent with some double-bond character.[6]

Experimental.—We had prepared cæsium tetrachlororuthenate for other studies. "Specpure" ruthenium metal and the other ruthenium compounds were from Johnson, Matthey & Co. Ltd. Commercial ruthenium trichloride and $[RuNO{\cdot}OH(NH_3)_4]Cl_2$ were analysed for ruthenium by reduction to metal,[7] the purity of which was established by spectrographic analyses. Commercial potassium perruthenate, dried at 110° (Found: K, 20·8; Ru, 45·6. (Calc. for $KRuO_4$: K, 19·1; Ru, 49·4%), had 3% of the ruthenium in a form other than ruthenate or perruthenate.

Isosbestic point at 415 mμ. Solutions containing known amounts of ruthenium were prepared (*a*) by gently boiling the trichloride (0·02 g.) and $[RuNO{\cdot}OH(NH_3)_4]Cl_2$ (0·03 g.) with 2M-potassium hydroxide (50 ml.) and potassium persulphate (0·25 g.) until the orange-red colour of ruthenate just changed to the green of perruthenate; (*b*) by fusing ruthenium metal (0·005—0·033 g.) at 500° with potassium hydroxide (0·15 g.) and potassium nitrate (0·25 g.) and dissolving the melt in 2M-potassium hydroxide (about 50 ml.) containing potassium persulphate (0·25 g.). Aliquot parts (10 ml.) from these stock solutions were boiled for different periods (1—4 min.) with more potassium persulphate (0·1 g.) to give different proportions of ruthenate and perruthenate and then diluted to 50 ml. with 2M-potassium hydroxide. Their spectra were measured between 400 and 420 mμ. The average value (1047) of ε_{Ru} at 415 mμ was constant in concentrations of alkali from 0·2M to 2M and in the useful range from 10^{-4}M- to 2×10^{-3}M-ruthenium and has been adopted for ruthenium determinations in these laboratories. Ruthenium was lost from boiling <2M-potassium hydroxide; in 6 min. a 0·2M-solution with $2{\cdot}14 \times 10^{-3}$M-Ru lost 26% and one of M-potassium hydroxide only 4%.

Ruthenate solutions. (*a*) Ruthenium metal (0·010—0·033 g.) was fused at 500° with potassium hydroxide and nitrate, and the melt extracted into cold 2M-potassium hydroxide (100 ml.). The optical density at 415 mμ showed that all the ruthenium was oxidised to Ru^{VI} or Ru^{VII}. (*b*) Cæsium tetrachlororuthenate(VI) (0·069 and 0·040 g.) was dissolved in 200 ml. of cold 2M-potassium hydroxide. To each ruthenate solution, potassium persulphate (~0·05 g.) was added to prevent the slow disproportionation which gives ruthenium dioxide. Absence of perruthenate was established by there being no change in D at 385 mμ in the presence of 0·05M-potassium iodide.

[4] Wehner and Hindman, *J. Amer. Chem. Soc.*, 1950, **72**, 3911.
[5] Barraclough, Lewis, and Nyholm, *J.*, 1959, 3552.
[6] Silverman and Levy, *J. Amer. Chem. Soc.*, 1954, **76**, 3317.
[7] Gilchrist, Raleigh, and Wichers, *J. Amer. Chem. Soc.*, 1935, **57**, 2567.

Perruthenate solutions. Ruthenate solutions (50 ml.; $\sim 2 \times 10^{-3}$M-Ru), prepared from $Cs_2[RuO_2Cl_4]$, were oxidised by boiling them for 3—6 min. with potassium persulphate (0·25 g.) in 0·1—1M-potassium hydroxide. The ruthenium concentrations of the cooled solutions were calculated from the optical density at 415 mμ to correct for loss of Ru^{VIII} by volatilisation. Contact with carbon tetrachloride showed the absence of Ru^{VIII} in the aqueous phase.

Spectra. Absorption spectra were measured in fused silica cells at 21°: with a Unicam S.P. 500 spectrophotometer, and the infrared spectrum for mulls in Nujol between rock-salt windows with a Hilger H.800 spectrophotometer fitted with a rock-salt prism.

We thank Professor R. E. Connick for discussions by correspondence and for suggesting the use of potassium iodide to test for the purity of ruthenate solutions.

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992. *The Cross-linking of Cellulose and its Derivatives. Part V.*[1] *The Stability of Some* N*-Substituted* β*-Aminobutyric Acids and their Esters.*

By W. M. CORBETT, J. E. MCKAY, and W. TAYLOR.

IN Part I of this series[2] the addition of amines to cellulose crotonate was shown to be a suitable means of controlled cross-linking of cellulose and its derivatives. This reaction leads to the formation of *N*-substituted β-aminobutyrates which in the presence of water at room temperature are known to undergo hydrolysis and, at higher temperatures, the resulting free acids revert to crotonic acid and the corresponding amine, thus:

$$NHR{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2R' \longrightarrow NHR{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H \longrightarrow CHMe{:}CH{\cdot}CO_2H + NH_2R$$

The elimination is not due to heat alone, for crotonic acid was not detected when the acids were heated alone at 100°, and it must be initiated by attack of water at the hydrogen atoms on the α-carbon atom. The stability of aqueous solutions of several *N*-substituted β-aminobutyric acids has been examined so that the effect of the nature of the *N*-substituent may be shown. The elimination was followed by addition of sulphuric acid to the β-amino-acid solutions, distillation of the crotonic acid at 50° under reduced pressure, and determination of the crotonic acid in the distillate by oxidation with potassium permanganate. This process causes a small amount of elimination (<0·5%).

An aqueous solution of *NN'*-ethylenedi-(β-aminobutyric acid) (I) at 50° undergoes degradation only very slowly (Table 1), but at 100° the reaction is more rapid, levelling off

TABLE 1.

Decomposition of aqueous *NN'*-ethylenedi-(β-aminobutyric acid).

Time (hr.) at 100°	0	1·5	3·7	6	8	13	19
Crotonic acid formed (equiv.)	0·034	0·224	0·292	0·311	0·332	0·340	0·338
Time (hr.) at 50°	2	4	6·3	8·5	12·5		
Crotonic acid formed (equiv.)	0·018	0·022	0·024	0·022	0·024		

after 12 hr. when 0·35 equiv. of crotonic acid per equiv. of acid (I) had been produced. After 19 hr. the dibasic acid was recovered in 40% yield, indicating that the main reaction was decomposition to the monobasic acid (II; $R = CH_2{\cdot}CH_2{\cdot}NH_2$) and crotonic acid. Paper chromatography of the residue gave spots corresponding to β-(2-aminoethylamino)-butyric acid (II; $R = CH_2{\cdot}CH_2{\cdot}NH_2$) and ethylenediamine, the latter in very small amounts. The decomposition of other *N*-substituted β-aminobutyric acids, prepared by

[1] Part IV, Corbett and Winters, *J.*, 1961, 4823.
[2] Corbett and McKay, *J. Soc. Dyers and Colourists*, in the press.

addition of ethanolamine, benzylamine, *N*-acetylethylenediamine, hexylamine, and 6-*O*-3′-aminopropyldi-*O*-isopropylidene-D-galactose [3] to crotonic acid are given in Fig. 1. Interference with the crotonic acid estimation, probably by the isopropylidene groups, was

$(\cdot CH_2 \cdot NH \cdot CHMe \cdot CO_2H)_2$ (I) $NHR \cdot CHMe \cdot CH_2 \cdot CO_2H$ (II) $NH(CHMe \cdot CH_2 \cdot CO_2H)_2$ (III)

observed for the carbohydrate derivative although crotonic acid could be determined satisfactorily in the presence of di-*O*-isopropylidene-D-glucose. In this case corrected values were obtained by deduction of the value given by extrapolation to zero time.

Fig. 1 shows that the stabilities of the acids vary considerably, but cannot be related directly to structure. Of interest is the carbohydrate acid which is relatively stable, decomposing at a rate similar to that of β-aminobutyric acid itself.

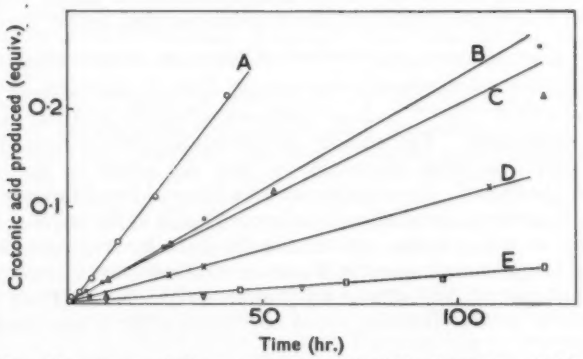
Hydrolysis of aqueous suspensions of ethyl β-benzylamino- and β-hexylamino-butyrate and of ββ′-iminodibutyrate [4] (III) has been followed by estimation of ethanol formed.

TABLE 2.

Hydrolysis of aqueous suspensions of esters.

	(II; R = CH_2Ph)			(II; R = n-C_6H_{13})			(III)		
Time (hr.)	5	24	100	7·25	24	77	5	27·5	74
EtOH formed (equiv.)	0·26	0·80	1·03	0·47	0·96	1·01	0·43	0·55	0·52

The first two react at a steady rate, being completely hydrolysed after 70 hr. (Table 2). In contrast, the ester of the dibasic acid undergoes rapid hydrolysis to about 50% completion



Decomposition of aqueous solutions of amino-acids (II) where R = (A) $HO \cdot CH_2 \cdot CH_2$, (B) CH_2Ph, (C) $NHAc \cdot CH_2 \cdot CH_2$, (D) n-hexyl, (E) □ H and ▽ 6-*O*-3′-aminopropyl-di-*O*-isopropylidene-D-galactose.

at which value it remains constant. This levelling off arises from neutralisation of the amino-group by acid liberated by hydrolysis of the first ester group with consequent disappearance of base catalysis.

Experimental.—Addition of n-hexylamine to ethyl crotonate. A solution of ethyl crotonate (30 g.) and n-hexylamine (30 g.) in absolute ethanol (100 ml.) was kept at room temperature for 6½ days and then evaporated. The resulting syrup was refluxed for 1 hr. with water (300 ml.) and then extracted with ether. Evaporation of the aqueous phase gave a residue which after several recrystallisations from ethanol–acetone–ether yielded β-*n-hexylaminobutyric acid* (9 g.), m. p. 154—155° (Found: C, 64·1; H, 11·2; N, 7·8. $C_{10}H_{21}NO_2$ requires C, 64·2; H, 11·2; N,

[3] Corbett and McKay, *J.*, 1961, 2930.
[4] Morsch, *Monatsh.*, 1932, **60**, 50.

7·5%). Distillation of the concentrated ether extract gave *ethyl* β-*n-hexylaminobutyrate* (32·0 g.), b. p. 89—90°/0·01 mm. (Found: C, 66·6; H, 11·7; N, 6·9. $C_{12}H_{25}NO_2$ requires C, 67·0; H, 11·7; N, 6·5%).

Addition of benzylamine to ethyl crotonate. A solution of ethyl crotonate (34·2 g.) and benzylamine (32·1 g.) in ethanol (100 ml.) was kept for 4½ days at room temperature, then concentrated to a syrup which partly crystallised. The syrup was mixed with ether and filtered, to give benzylamine crotonate (0·4 g.), m. p. 85—91°: after two recrystallisations from ethyl acetate–light petroleum (b. p. 40—60°) (Found: C, 67·9; H, 7·7; N, 7·2. Calc. for $C_{11}H_{15}NO_2$: C, 68·4; H, 7·8; N, 7·3%). Evaporation of the ether solution gave a syrup which was refluxed for 1 hr. with water (300 ml.), then extracted with ether. The aqueous phase, on evaporation, gave a solid which after recrystallisation from ethanol–acetone–ether gave β-*benzylaminobutyric acid* (14 g.), m. p. 178—179° (Found: C, 68·4; H, 7·9; N, 7·4. $C_{11}H_{15}NO_2$ requires C, 68·4; H, 7·8; N, 7·3%). Evaporation of the ether extract gave a syrup which distilled at b. p. 110—117°/0·05 mm. to give *ethyl* β-*benzylaminobutyrate* (22 g.) (Found: C, 70·9; H, 8·8; N, 6·3. $C_{13}H_{19}NO_2$ requires C, 70·7; H, 8·7; N, 6·3%).

Decomposition of N-*substituted* β-*aminobutyric acids.* Samples were withdrawn periodically from refluxed 0·1N-aqueous solutions of the acids, and, after addition of an equal volume of 0·1N-sulphuric acid, were distilled under reduced pressure at 50° with intermittent addition of water (100 ml.). The crotonic acid in the distillate was measured by oxidation with an excess of potassium permanganate. This methodg ave 95% recovery when applied to standard crotonic acid solutions.

Hydrolysis of N-*substituted ethyl* β-*aminobutyrates* (With Mr. B. Sagar). Samples from agitated 0·1N-aqueous suspensions of the esters were chromatographed at 27° on a Pye argon chromatograph (column 4 ft.) comprising 120—150 mesh ballotini containing 0·7% of Flexol plasticiser 8N8 (Union Carbide Co.). The areas of the ethanol peaks were estimated by the triangulation method, and compared with that obtained for 0·1M-aqueous ethanol.

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993. *Oxaloacetic Acid. Part I. The Nature of Oxaloacetic Acid in the Solid State and in Neutral, Aqueous Solution.*

By Barbara E. C. Banks.

Two isomeric forms of crystalline, enolic oxaloacetic acid are reported to have m. p. 152° (*cis*) and 182° (*trans*).[1-3] The keto-acid has not been obtained crystalline. Meyer[4] showed, by bromine titration, that oxaloacetic acid is largely ketonic in aqueous solution. His estimate of the proportion (16—20%) of the enolic form present at equilibrium is, however, at variance with the value obtained by Hantzsch[5] (3%) from ultraviolet-absorption measurements. Gruber *et al.*[6] recently found that the two allegedly isomeric forms had identical infrared spectra and suggested, on this basis, that the difference in melting point was due only to the presence of traces of solid keto-acid as impurity.

[1] Wohl and Oesterlin, *Ber.*, 1901, **34**, 1139.
[2] Wohl, *Ber.*, 1907, **40**, 2282.
[3] Michael and Bucher, *Ber.*, 1896, **29**, 1792; *Ber.*, 1895, **28**, 2511.
[4] Meyer, *Ber.*, 1912, **45**, 2860.
[5] Hantzsch, *Ber.*, 1915, **48**, 1407.
[6] Gruber, Pfleiderer, and Wieland, *Biochem. Z.*, 1956, **328**, 245.

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Wohl and Oesterlin's method of preparation [1] of the two crystalline forms of oxaloacetic acid is by decomposition of the pyridine salt of hydroxymaleic anhydride by 12% or 30% sulphuric acid giving, respectively, solids melting at 152° and 180°. In our hands, consistently with the report by Gruber *et al.*, no true melting points can be observed. Materials having a continuous range of decomposition points (144—172°) are obtained by varying the sulphuric acid concentration. Further, the decomposition point of the supposed low-melting modification can be raised by recrystallisation from solvents containing traces of sulphuric acid (Table 4). Decomposition points were measured in a conventional melting point aparatus and were unaffected by exhaustive drying of the samples (*in vacuo*, over P_2O_5) or by treatment of the glass melting-point tubes with acid. Recrystallisation of oxaloacetic acid from solvents containing traces of hydrochloric acid, acetic acid, pyridine, or triethylamine was without effect on the decomposition point. Traces of methanesulphonic acid and dimethyl sulphate produced effects qualitatively similar to, though smaller than, those of sulphuric acid.

All crystalline samples of oxaloacetic acid (decomp. point 144—172°) had identical infrared spectra. Two samples (decomp. 144° and 172°) were found to have identical crystal powder diagrams. It is, therefore, concluded that the variation in decomposition point is of complex origin and does not indicate the existence of two distinct, solid, isomeric forms.

When solid oxaloacetic acid is dissolved in an aqueous buffer solution, a rapid decrease in ultraviolet absorption is observed, due to formation of the keto-acid. Gruber *et al.* determined the rate of ketonisation by reducing the keto-acid, as it was formed, by the coenzyme DPNH under the influence of an excess of the enzyme malic dehydrogenase.* The rate of the enzymic reduction is then equal to the rate of ketonisation of the substrate. In the present work, a less cumbersome, direct spectrophotometric technique has been used. The following points have been established. (*a*) The molar extinction coefficient, $\varepsilon_{280\ m\mu}$ (enol), of the enolic form of oxaloacetic acid, obtained by extrapolation of the optical data, does not vary with decomposition point. The view [6] that the variation of the decomposition point is due to the presence of traces of the keto-acid is, therefore, unfounded. (*b*) The extrapolated value of $\varepsilon_{280\ m\mu}$ (enol) is in fair agreement with the molar extinction coefficient of oxaloacetic acid in ether, in which solvent the acid is known to be enolic.[4,5] (*c*) The rate of ketonisation is, as would be expected, buffer-catalysed and pH-dependent. A detailed study of the kinetics of this process will be reported later.

The equilibrium molar extinction coefficient of oxaloacetic acid has been determined in a number of buffer solutions in the pH range 5·0—10·0 and in solutions of sodium hydroxide (Table 3). The higher values obtained in borate buffer are, presumably, due to complex formation between the enolic acid and borate.[7] Formation of a Schiff's base between the keto-acid and the unsubstituted amino-group of 2-amino-2-hydroxymethylpropane-1,3-diol (Tris) may account for the rather higher values of $\varepsilon_{280\ m\mu}$ in this buffer than in phosphate buffer at the same pH. The large increase in absorption in 0·1N-sodium hydroxide is presumably due to ionisation of the enolic hydroxyl group.

If the extinction coefficient of the keto-acid is assumed to be of the same order as that of the next higher homologue, α-oxoglutaric acid, values of the tautomeric equilibrium constant, $K = c_{enol}/c_{keto}$, can be computed from the optical data. In buffers other than borate or Tris, K is constant (corresponding to 15·5—16% of enol) in the pH range 5·0—10·0.

The amount of enol present at equilibrium has also been determined by bromine titration, by the method described. The value obtained in this way (15·5—15·8%) is in excellent agreement with that computed from the optical data.

* It is known that the keto-form of oxaloacetic acid is the biologically active substrate for this enzyme.

[7] Greenwood and Greenbaum, *Biochem. Biophys. Acta*, 1953, **10**, 623.

The isomeric form of the solid oxaloacetic acid has not been certainly identified but the absence of a peak, in the infrared spectrum, in the region of the normal OH stretching frequency (2·8 μ) suggests that the enolic hydroxyl group is strongly hydrogen-bonded. This would be the case for the *trans*-enolic isomer.

TABLE 1.

t (sec.)	Optical density (280 mμ)	$10^3(k_1 + k_{-1})$ (sec.$^{-1}$)	t (sec.)	Optical density (280 mμ)	$10^3(k_1 + k_{-1})$ (sec.$^{-1}$)
0	1·202	—	207	0·534	5·39
25	1·083	5·10	235	0·487	5·37
52	0·962	5·30	280	0·427	5·39
85	0·843	5·26	340	0·366	5·38
115	0·743	5·38	430	0·303	5·38
146	0·662	5·35	499	0·277	5·42
175	0·594	5·39	∞	0·206	

TABLE 2.

Temp.	1·5°	1·5°	1·5°	1·5°	12·0°	25·0°
Phosphate (M)	0·100	0·075	0·050	0·025	0·100	0·100
$10^3(k_1 + k_{-1})$ (sec.$^{-1}$)	5·34	3·66	2·36	1·27	~15	~56
$\varepsilon_{280\ m\mu}$ (enol)	3430	3320	3430	3360	—	—

Experimental and Results.—Oxaloacetic acid was prepared from tartaric acid by Wohl and Oesterlin's method.[1] The product was recrystallised from hot acetone by the addition of hot benzene (Found: C, 37·0; H, 3·3; equiv., 131. Calc. for $C_4H_4O_5$: C, 36·4; H, 3·8%; equiv., 132). Buffer solutions were prepared from " AnalaR " reagents, except commercial 2-amino-2-(hydroxymethyl)propane-1,3-diol.

Ultraviolet absorption techniques. Measurements were made on a Unicam S.P. 500 spectrophotometer fitted with a temperature-controlled cell holder. The absorption changes occurring on dissolving oxaloacetic acid in aqueous buffer at neutral pH's were followed by a modification of the method of Gruber *et al.*[6] A small amount of the solid (*ca.* 0·025 g.) was dissolved in ethanol (5 c.c.) at −10°. An aliquot part (0·025 c.c.) of the ethanol solution was added to the buffer (3 c.c.) in a 1 cm. stoppered silica cell in the cell holder. The optical density (at 280 mμ) was determined at suitable time intervals. Below room temperature, dry nitrogen was blown through the cell holder to prevent misting on the optical surfaces. The sum of the first-order rate coefficients for ketonisation (k_1) and enolisation (k_{-1}) was calculated from the equation

$$k_1 + k_{-1} = \frac{2{\cdot}303}{t} \log \frac{D_0 - D_{eq}}{D_t - D_{eq}},$$

where t is the time (sec.) and D_0, D_{eq}, and D_t are the optical densities (280 mμ) at zero time, equilibrium, and t seconds respectively. Table 1 shows the results of a typical kinetic run, in 0·1M-phosphate buffer (pH 7·38) at 1·5°.

Table 2 gives the values of $(k_1 + k_{-1})$ at different concentrations of phosphate buffer (pH 7·38) and different temperatures in 0·1M-phosphate buffer together with values of $\varepsilon_{280\ m\mu}$ (enol) obtained by extrapolation of the optical data at the lowest temperature.

The equilibrium molar extinction coefficients of oxaloacetic acid in a number of buffer solutions and in solutions of sodium hydroxide are given in Table 3.

Bromination method. Oxaloacetic acid (0·16—0·25 g.) was dissolved in 0·1M-phosphate buffer (5 c.c.; pH 7·38) and allowed to reach tautomeric equilibrium (30 min., 25°). An aliquot part (4 c.c.) of the equilibrated solution was added to a slight excess (6 c.c.) of methanolic ~0·1N-bromine (containing M-lithium bromide) precooled to −20°. After varying times (30—120 sec.) the excess of bromine was removed by addition of di-isobutylene (4 c.c.). An excess of 10% aqueous potassium iodide (20 c.c.) was added and the solution left at 25° for

TABLE 3.

Buffer	pH	$\varepsilon_{280\ m\mu}$	Buffer	pH	$\varepsilon_{280\ m\mu}$	Buffer	pH	$\varepsilon_{280\ m\mu}$
Acetate	5·00	540	Phosphate ...	8·00	542	CO_3^{2-}–HCO_3^-	9·89	535
Phosphate ...	5·90	535	Tris	7·50	625	Borate	9·20	1,447
Phosphate ...	6·43	533	Tris	8·29	635	Borate	9·81	929
Phosphate ...	6·92	543	Tris	9·08	594	0·01N-NaOH...		659
Phosphate ...	7·38	550	CO_3^{2-}–HCO_3^-	9·28	548	0·1N-NaOH ...		1,950

$\varepsilon_{280\ m\mu}$ of oxaloacetic acid in ether is 3320. $\varepsilon_{280\ m\mu}$ of α-oxoglutaric acid in phosphate buffer (0·1M; pH 7·38) is 24.

TABLE 4.

Vol. H_2SO_4/100 c.c. of acetone	0·05	0·08	0·10	0·12	0·14	0·20	0·30
Decomp. pt. (corr.)	163°	165°	167°	162°	159°	151°	147°

30 min. The liberated iodine was titrated with 0·1N-sodium thiosulphate (soluble sodium–starch glycollate indicator).

Bromination was complete in 90 sec. at −20°. The percentage of enol estimated by this method was 15·5—15·8%.

Decomposition points. Table 4 shows the change in decomposition point on recrystallisation of a sample of oxaloacetic acid originally decomposing at 151°, from acetone–benzene containing traces of sulphuric acid.

Infrared spectra. These were measured for Nujol mulls on the Perkin-Elmer Infracord and on the Grubb-Parsons infrared spectrometers. The main absorption peaks occur at 1723, 1697, 1638, 1429, 1266, and 1235 cm.$^{-1}$.

Powder diffraction photographs. These were taken on a Phillips powder camera with Cu-$K\alpha$ radiation.

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994. *Solvent extraction of Septivalent Rhenium. Part III.*[1] *Heterogeneous Equilibria in the System, Aqueous Nitric Acid–Potassium Perrhenate–Dibutyl Phosphate.*

By AVIEZER STEVAN KERTES and ANNA BECK.

THIS paper extends our earlier work [1] on extraction of rhenium(VII) by tributyl phosphate and tri-iso-octylamine to cover, in all, three types of extractants: those extracting inorganic species by molecular association (Bu_3PO_4); those involving anion-exchange mechanism (R_3N); and those involving a cation-exchange mechanism (Bu_2HPO_4).

The two previous papers suggest that the rhenium-bearing species is exclusively the undissociated, or ion-paired, perrhenic acid, $HReO_4$, which is probably a general phenomenon for the metal oxy-acids.[2] In dealing with the extraction of perrhenic acid from aqueous nitric acid solutions, not only the rhenium(VII) species has to be considered, but also the extraction of nitric acid. Consequently, the system discussed in this series of papers is similar to those dealing with the extraction of strong complex acids of the type $HM^{III}X_4$ from strong mineral acids HX, where co-extraction of two strong acids has to be considered. Now, the extraction ratio of either of these acids from the aqueous phase containing a mixture of the two into dibutyl hydrogen phosphates will depend mainly on two factors: (i) the relative free-energy change favourable for the transfer of the ion-pairs into the solvent phase, and (ii) the mass-action effect in the aqueous phase. It seems to be of interest, therefore, to study, first, the simpler two-phase system of only three components, namely, water, nitric acid, and dibutyl hydrogen phosphate. The results, recently summarised,[3] on the solute–solvent interaction in the above system, showed that the molecular species existing in the organic phase when in equilibrium with aqueous nitric acid up to about 9M, are only the dimer dihydrate $(Bu_2HPO_4,H_2O)_2$ and a molecular adduct of the composition $(Bu_2HPO_4,H_2O)_2,HNO_3$ to the virtual exclusion of other species. The above nitric acid solvate is formed by the following reaction (water of hydration being omitted for simplicity):

$$(Bu_2HPO_4)_{2,o} + HNO_{3,a} \longrightarrow (Bu_2HPO_4)_2,\ HNO_{3,o} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

[1] Parts I and II, *J.*, 1961, 1921, 1926.
[2] Knapp, Smutz, and Spedding, ISC–766, 1957; Gerlit, Proc. Internat. Conf. Peaceful Uses of Atomic Energy, Geneva, 1955, United Nations, Vol. VII, p. 145.
[3] Kertes, Beck, and Habousha, *J. Inorg. Nuclear Chem.*, in the press.

and for the corresponding equilibrium quotient the value $K_{HNO_3} = 2{\cdot}1$ has been calculated. (The subscripts o and a refer to the organic and the aqueous phase, respectively. $HNO_{3,a}$ refers to undissociated acid.)

The experimental results for the distribution of perrhenate between aqueous nitric acid and undiluted dibutyl hydrogen phosphate (4·85M) or mixtures of this with carbon tetrachloride are shown in Fig. 1 as a function of the concentration of nitric acid in the initial aqueous solution. The total concentration of rhenium originally in the aqueous solution was $1{\cdot}8 \times 10^{-2}$M in all the experiments shown. The experiments were extended

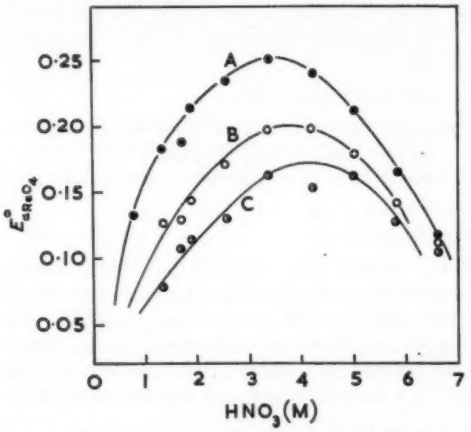

FIG. 1. Extraction ratio of perrhenate with changing nitric acid concentration in the initial aqueous solution : dibutyl hydrogen phosphate concentration = (A) 4·85M, (B) 4·36M, and (C) 3·88M.

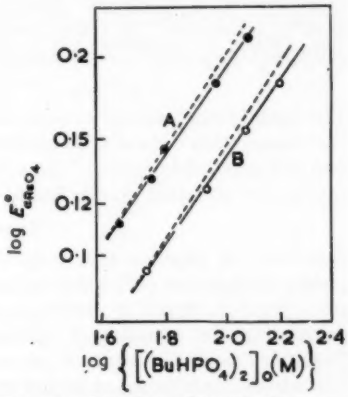

FIG. 2. Log–log plot of the perrhenate extraction ratio against $[Bu_2HPO_4)_2]_o$ for (A) 1·88M- and (B) 1·34M-nitric acid. The broken lines are drawn with a slope of 3.

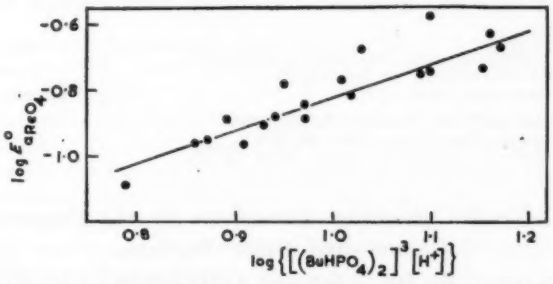

FIG. 3. Log–log plot of the perrhenate extraction ratio against $[(Bu_2HPO_4)_2]_o^3[H^+]_a$ for 4·85M-, 4·36M-, and 3·88M-dibutyl hydrogen phosphate and nitric acid concentrations up to 3·34M in the initial aqueous solution. The three most divergent points are those for the highest nitric acid concentrations.

to higher and lower nitric acid concentrations than those shown in the Figure, and also to dibutyl hydrogen phosphate concentrations lower than 3·88M, but the difficulties involved in the analytical determinations of rhenium in very low concentration in the organic phase render the measurements of very low $E_a°$ values unreliable. The curves are similar in shape to the graph with tributyl phosphate instead of dibutyl hydrogen phosphate, but the maximum occurs at a different concentration of acid. The solvation number of rhenium(VII) in the ester phase was found by the slope of a log–log plot of $E_a°$ against the concentration of free dibutyl hydrogen phosphate, *i.e.*, the portion of the ester not engaged in the nitric acid adduct, as calculated by assuming [3] complete formation of

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$(Bu_2HPO_4)_2,HNO_3$ in the equilibrium organic phase at constant nitric acid concentration. The straight lines in Fig. 2, representing this graph, show a slope of nearly 3, suggesting that a trisolvate of rhenium extractable species exists in the ester phase. The above results suggest that the reaction

$$3(Bu_2HPO_4)_{2,o} + HReO_{4,a} \longrightarrow \{(Bu_2HPO_4)_2\}_3,HReO_{4,o} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

represents the extraction mechanism of rhenium by dibutyl hydrogen phosphate. The amounts of undissociated perrhenic acid in the presence of various high concentrations of nitric acid could not be calculated from the results presented in this paper, nor are they available from elsewhere (they must be very different from those in perchloric acid [4]); therefore, in order to evaluate the formation constant of the compound $\{(Bu_2HPO_4)_2\}_3,HReO_4$, equation (2) was rewritten as

$$3(Bu_2HPO_4)_{2,o} + H^+_a + ReO^+_{4,a} \longrightarrow \{Bu_2HPO_4)_2\}_3,HReO_{4,o} \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The equilibrium quotient of equation (3) differs from that of equation (2) in that it includes the dissociation constant of perrhenic acid. As the ratio $\{(Bu_2HPO_4)_2\}_3,HReO_4 : ReO_4^-$ can be expressed in terms of the measured extraction ratio of rhenium(VII), the equilibrium quotient of equation (3) can finally be written as

$$K_{HReO_4} = E_a^\circ/[(Bu_2HPO_4)_2]_o^3[H^+]_a \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Equation (4) requires that a graph of log E_a° against log $[(Bu_2HPO_4)_2]_o^3[H^+]_a$ should yield a straight line with a slope of unity and an intercept on the ordinate axis representing pK. Such a graph is shown in Fig. 3, with p$K = 1{\cdot}796$, *i.e.*, $K_{HReO_4} = 0{\cdot}016$. In calculating the equilibrium quotient, no significant trend was observed up to about 3M-nitric acid in the aqueous phase, but it has become increasingly apparent that serious limitations are imposed at higher acid content by a lack of determined activity coefficients for the organic solutes.

In conclusion, it may be said that dibutyl hydrogen phosphate and presumably other dialkyl hydrogen phosphates, have a low affinity for perrhenic acid, which seems to be a fairly general phenomenon for metal oxy-acids.[5] Further, it seems reasonable to suggest that dialkyl hydrogen phosphates act as trialkyl phosphates in the extraction of mineral acids [6] by forming molecular species in the organic phase without involving an ion-exchange mechanism.

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[*Received, May 18th*, 1961.]

[4] Bailey, Carrington, Lott, and Symons, *J.*, 1960, 290.
[5] Boyd and Larson, *J. Phys. Chem.*, 1960, **64**, 988.
[6] Dyrssen and Kraśovec, *Acta Chem. Scand.*, 1959, **13**, 561.

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995. *A Novel Cyclisation Procedure for the Preparation of Chloro- and Other Purines.*

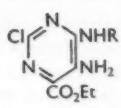
By JIM CLARK and J. H. LISTER.

BRIEF mention has already been made of the use of a mixture of dimethylformamide and phosphoryl chloride for conversion of 4,5-diaminopyrimidines into purines.[1] Other purines have now been synthesised in the same way and the procedure has been shown to be particularly useful for the direct preparation of purines with a chlorine atom in the pyrimidine ring. Such compounds have previously been made by heating 4,5-diamino-chloropyrimidines, under reflux, with diethoxymethyl acetate [2] or a mixture of ethyl orthoformate and acetic anhydride.[3]

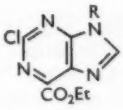
A feature of the new method is the ease with which very weakly basic diamines are converted into purines under mild conditions. This is illustrated by cyclisation of the

[1] Clark and Ramage, *J.*, 1958, 2821.
[2] Montgomery and Temple, *J. Amer. Chem. Soc.*, 1957, **79**, 5238; Montgomery and Holum, *ibid.*, 1958, **80**, 404.
[3] Montgomery, *J. Amer. Chem. Soc.*, 1956, **78**, 1928.

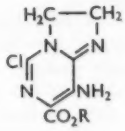
2-chloropyrimidines (I—III) to the corresponding purines (IV—VI). Ethyl 4,5-diamino-2-chloropyrimidine-6-carboxylate * (I) in particular is very unreactive and does not condense with 1,2-dicarbonyl compounds although reactions of this type form the basis of the very widely used Isay synthesis of pteridines.[4] For example, the compound was recovered after being heated for several hours with polyglyoxal in boiling 2-ethoxyethanol. In spite of this the diamine (pK_a 2·6), which is about 2500 times less basic than 4,5-diaminopyrimidine (pK_a 6·0),[5] was readily cyclised to the purine by dimethylformamide and phosphoryl chloride. Another diamine (II) which is about 1000 times less basic still (pK_a <0) was equally readily cyclised by the same method, in excellent yield. In the case of the 5-amino-4-2′-chloroethylaminopyrimidine (III) the purine synthesis succeeded in spite of competition from an alternative cyclisation which would have yielded the imidazolopyrimidine (VII).[1]



(I)



(IV)

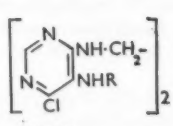


(VII)

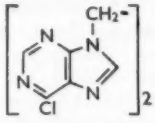
(II) R = $CH_2 \cdot CO_2Et$ (V)

(III) R = $CH_2 \cdot CH_2Cl$ (VI)

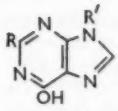
In certain cases the new method has proved successful with 4,5-diaminopyrimidines which did not give purines with the more usual cyclising agents. For example, although acetic anhydride–ethyl orthoformate and the 1,2-dipyrimidinylaminoethane (VIII; R = H) gave only the diacetamido-derivative (VIII; R = Ac),[6] the phosphoryl chloride–dimethylformamide mixture gave the required purine (IX) in very good yield.



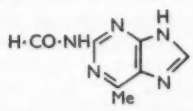
(VIII)



(IX)



(X)



(XI)

The method appears to be generally applicable, provided no group liable to attack by the reagents is present. The conditions are so mild as to leave nuclear hydroxyl groups unchanged, thus both xanthine (X; R = OH, R′ = H) and a derivative of hypoxanthine (X; R = H, R′ = cyclohexyl) have been prepared from suitable hydroxypyrimidines. The 2-formamidopurine (XI) was obtained from 2,4,5-triamino-6-methylpyrimidine.

Although generally the heat of reaction produced by adding the phosphoryl chloride to the diaminopyrimidine–dimethylformamide mixture appears to be sufficient, in some cases heating on the water bath may be necessary to complete the reaction. Working up is very simple and usually consists of reducing the volume of the mixture, adding ice or water, and adjusting the pH as required.

This method of supplying the 8-carbon atom of a purine is an extension of the Vilsmeier–Haack formylation [7] which is an established procedure for the introduction of aldehyde groups into reactive heterocyclic nuclei. Another variant of this reaction, in which *o*-formamido-thioamides were cyclised to 4-mercaptopyrimidines by treatment with dimethylformamide and hydrogen chloride, was recently reported to give better yields than existing methods.[8]

Experimental.—Ethyl 2-chloropurine-6-carboxylate (IV). A mixture of ethyl 4,5-diamino-2-chloropyrimidine-6-carboxylate (0·2 g.), freshly distilled *NN*-dimethylformamide (10

* The synthesis of this compound and some physical data will be published shortly.

[4] Isay, *Ber.*, 1906, **39**, 250; Albert, *Quart. Rev.*, 1952, **6**, 225.
[5] Albert, *J.*, 1955, 2690.
[6] Lister, unpublished work.
[7] Vilsmeier and Haack, *Ber.*, 1927, **60**, 119; Minkin and Dorofeenko, *Uspekhi Khim.*, 1960, **29**, 1301.
[8] Taylor and Zoltewicz, *J. Amer. Chem. Soc.*, 1961, **83**, 248.

XUM

ml.), and phosphoryl chloride (1 ml.) was set aside for 1 hr., then heated on the water bath for 0·25 hr. Volatile matter was removed, under reduced pressure, on the water bath and the residue was treated with cold water (10 ml.) and a little dilute aqueous ammonia. *Ethyl 2-chloropurine-6-carboxylate* (0·16 g.) was filtered off and crystallised from 2-ethoxyethanol (charcoal) as plates, m. p. 254° (decomp.) (Found: C, 42·4; H, 2·9; N, 24·0. $C_8H_7ClN_4O_2$ requires C, 42·4; H, 3·1; N, 24·7%), exhibiting a slight blue fluorescence in ultraviolet (Wood's) light.

Ethyl 2-chloro-6-ethoxycarbonyl-9-purinylacetate (V). A mixture of ethyl 5-amino-2-chloro-6-ethoxycarbonyl-4-pyrimidinylaminoacetate [9] (II) (0·5 g.), *NN*-dimethylformamide (10 ml.), and phosphoryl chloride (1 ml.) was treated as described above except that no ammonia was required. Almost pure *ethyl 2-chloro-6-ethoxycarbonyl-9-purinylacetate* (0·43 g.), m. p. 134°, was obtained; this crystallised from ethanol as plates, m. p. 135° (Found: C, 45·9; H, 4·2. $C_{12}H_{13}ClN_4O_4$ requires C, 46·1; H, 4·2%), giving a slight blue fluorescence in ultraviolet (Wood's) light.

1,2-Di-(6-chloro-9-purinyl)ethane (IX). 1,2-Di-(5-amino-4-chloro-6-pyrimidinylamino)-ethane [6] (4·7 g.) in *NN*-dimethylformamide (40 ml.) was treated slowly with phosphoryl chloride (10 ml.), with some cooling, and left for 2 hr. The mixture was taken to dryness and the residue treated with ice (25 g.). The clear solution quickly deposited a yellow crystalline product (4·7 g., 82%) which on recrystallisation from propan-1-ol gave *1,2-di-(6-chloro-9-purinyl)ethane* as colourless needles, m. p. 284—286° (Found: C, 43·5; H, 2·6; N, 33·6. $C_{12}H_8Cl_2N_8$ requires C, 43·0; H, 2·4; N, 33·5%).

9-Cyclohexylhypoxanthine [10] (X; R = H, R′ = cyclohexyl). Phosphoryl chloride (0·5 ml.) was added to a solution of 5-amino-4-cyclohexylamino-6-hydroxypyrimidine (0·5 g.) in dimethylformamide (5 ml.), and the mixture was treated as above. The resulting aqueous solution was brought to pH 6 and refrigerated overnight. The crude product was filtered off (0·4 g., 76%) and recrystallised from water, giving *9-cyclohexylhypoxanthine* as prisms, m. p. 274—276° (Found: C, 60·2; H, 6·4; N, 25·6. $C_{11}H_{14}N_4O$ requires C, 60·5; H, 6·5; N, 25·7%).

2-Formamido-6-methylpurine (XI). A mixture of 2,4,5-triamino-6-methylpyrimidine (1 g.), dimethylformamide (12 ml.), and phosphoryl chloride (2 ml.) was treated as above. The *product* crystallised from water as colourless prisms (0·15 g.), m. p. >300° (Found: C, 47·75; H, 4·2; N, 39·2. $C_7H_7N_5O$ requires C, 47·3; H, 4·0; N, 39·5%).

Xanthine (X; R = OH, R′ = H). Obtained from 4,5-diamino-2,6-dihydroxypyrimidine as above, the product crystallised from water (charcoal) and agreed in analysis and ascending chromatography (in ammonium hydrogen carbonate solution [11]) with an authentic sample of xanthine (R_F 0·45) (Found: C, 39·3; H, 2·5. Calc. for $C_5H_4N_4O_2$: C, 39·5; H, 2·65%).

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[9] Clark and Layton, *J.*, 1959, 3411.
[10] Montgomery and Temple, *J. Amer. Chem. Soc.*, 1958, **80**, 409.
[11] Hems, *Arch. Biochem. Biophys.*, 1959, **82**, 485.

996. *The Preparation of Ammonium Alkyl Hydrogen Phosphites.*

By T. D. Smith.

The general method for the preparation of ammonium salts of organic phosphorous acids consists of the ammonolysis of organic phosphites in a suitable solvent or the treatment of the barium salt with ammonium sulphate. Diammonium iso-octyl phosphate [1] has been prepared by passing ammonia into a mixture of phosphorus pentoxide and iso-octyl alcohol, whilst the ammonolysis of pentaethyl tripolyphosphate in chloroform gives ammonium diethyl phosphate, ethyl hydrogen phosphoramidate, and diethylphosphoramide.[2,3]

[1] Rudel and Gargisa, U.S.P. 2,791,495.
[2] Simon and Stölzer, *Chem. Ber.*, 1956, **89**, 2253.
[3] Rätz and Thilo, *Z. anorg. Chem.*, 1953, **272**, 333.

In a study of the structure of organic acid phosphates the reaction of dialkyl hydrogen phosphites with ammonium thiocyanate was investigated:

$$PHO(OR)_2 + NH_4{\cdot}SCN \longrightarrow PHO(OR)(ONH_4) + RSCN$$

Previous studies [4] involving alkylation by dialkyl phosphites indicated that trialkyl phosphates react similarly; trialkyl phosphates reacted with ammonium thiocyanate to yield ammonium dialkyl phosphates.

Experimental.—Ammonium thiocyanate (0·04 mole) was heated at 125° with the dialkyl hydrogen phosphite (0·04 mole) for 4 hr. With dimethyl hydrogen phosphite the upper phase was separated, washed with 10% aqueous potassium carbonate, and water; it was distilled, and identified as methyl thiocyanate (1·9 g.), b. p. 130°.

The lower phase was treated with acetone (200 ml.), and the ammonium alkyl hydrogen phosphite separated. After filtration, the residue was washed with dry ether, recrystallised from acetone–ethanol, pumped until free of solvent, and stored over phosphorus pentoxide. The salient features of the various syntheses are detailed in the Table.

Product	Yield (%)	M. p.	Found (%) C	Found (%) P	Found (%) N	Reqd. (%) C	Reqd. (%) P	Reqd. (%) N
$(NH_4)MeHPO_3$ ...	92	108	10·6	27·4	12·4	10·7	27·3	12·3
$(NH_4)EtHPO_3$ ...	80	94	18·9	24·4	11·0	18·6	24·2	10·8
$(NH_4)Pr^iHPO_3$ ...	53	37	25·5	22·0	9·9	25·7	21·8	9·7
$(NH_4)Bu^nHPO_3$ ...	28	87	31·0	20·0	9·0	31·2	19·6	8·9
$(NH_4)Me_2PO_4$	74	103	16·8	21·7	9·8	16·7	21·5	9·8
$(NH_4)Et_2PO_4$	59	102	28·7	18·1	8·2	28·4	17·9	8·1

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[4] Smith and Parker, *J.*, 1961, 442.

997. *The Disproportionation of Carbodi-imides.*

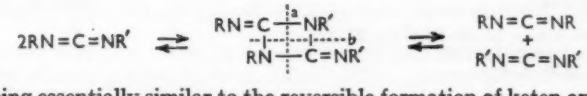
By I. G. HINTON and R. F. WEBB.

IN a study of potential cross-linking agents for polymer systems we have examined the preparation and properties of a series of biscarbodi-imides, the nitrogen analogues of the technically important di-isocyanates. The carbodi-imides were prepared by condensation of diamines such as ethylene-, hexamethylene-, and *m*-phenylene-diamine with alkyl isothiocyanates and dehydrosulphurisation of the resulting thioureas by mercuric oxide. The crude biscarbodi-imides were obtained as oils and characterised by conversion in high yield into the crystalline bisureas by treatment with glacial acetic acid.

Attempted distillation of the crude biscarbodi-imides gave only symmetrical carbodi-imides and involatile polymeric residues; thus hexamethylenebis(cyclohexylcarbodi-imide) gave dicyclohexylcarbodi-imide and an involatile polymer, presumably poly-(hexamethylenecarbodi-imide). At lower temperature and pressure certain biscarbodi-imides, *e.g.*, tetramethylenebis-(t-butylcarbodi-imide) can be distilled unchanged.[1]

The thermal disproportionation has been confirmed for the unsymmetrical carbodi-imide, isopropylphenylcarbodi-imide, which distilled unchanged at 110°/14 mm. but when distilled at atmospheric pressure gave di-isopropylcarbodi-imide and diphenylcarbodi-imide.

The disproportionation probably proceeds through the formation of cyclic dimers (or trimers) [2] which depolymerise with bond fission at a or b: as shown for the dimer:



the reaction being essentially similar to the reversible formation of keten and allene dimers.

[1] G.P. 924,751/1955.
[2] Khorana, *Chem. Rev.*, 1953, **53**, 145.

Continuous removal of a lower-boiling symmetrical carbodi-imide from the equilibrium mixture will drive the disproportionation to completion.

Experimental.—Hexamethylenebis(cyclohexylthiourea). Cyclohexyl isothiocyanate (40 g.) and 70% aqueous hexamethylenediamine (23·8 g.) in acetone (200 ml.) were left at room temperature for 15 hr. The solvent was evaporated *in vacuo*, and the residue washed with light petroleum (b. p. 40—60°) and recrystallised from methanol to give the *bisthiourea* (55 g.), m. p. 143—145° (Found: C, 60·4; H, 9·6; N, 13·7; S, 16·1. $C_{20}H_{38}N_4S_2$ requires C, 60·2; H, 9·6; N, 14·1; S, 16·1%).

Hexamethylenebis(cyclohexylcarbodi-imide). The bisthiourea (40 g.) and yellow mercuric oxide (250 g.) were suspended in boiling carbon disulphide (500 ml.) and stirred under reflux for 20 hr. Powdered calcium chloride (40 g.) and Hyflo Supercel (50 g.) were added; the mixture was filtered and evaporated. The residual oil (24 g.) was taken up in light petroleum (b. p. 40—60°), shaken with Hyflo Supercel, filtered to remove unchanged thiourea, and evaporated, leaving the crude biscarbodi-imide as a yellow oil (19 g.), $\nu_{max.}$ 2150 cm.$^{-1}$.

When the crude carbodi-imide (4 g.) was dissolved in glacial acetic acid (20 ml.) the solution became hot and deposited colourless crystals; the mixture was poured into cold water (100 ml.), and the solid (3·8 g.) collected, washed with boiling acetone, recrystallised from glacial acetic acid, washed with acetone, and dried to give *hexamethylenedi(cyclohexylurea)*, m. p. 230—232° (Found: C, 65·3; H, 10·3. $C_{20}H_{38}N_4O_2$ requires C, 65·5; H, 10·4%).

Disproportionation of the biscarbodi-imide. The crude biscarbodi-imide was distilled, first at 14 mm. through a 20″ Vigreux column, to give materials (*a*) (2·9 g.), b. p. 100°/14 mm., cyclohexyl isothiocyanate produced in a side reaction, and (*b*) (2·4 g.), b. p. 150—154°/14 mm., dicyclohexylcarbodi-imide. The residue was further distilled at 0·35 mm. without the column to give materials (*c*) (1·6 g.), b. p. 91—92°/0·35 mm., dicyclohexylcarbodi-imide, (*d*) (3·9 g.), b. p. 92—200°/0·35 mm., mainly hexamethylenebis(cyclohexylcarbodi-imide), and (*e*) (2·5 g.), a black residue. On treatment with acetic acid, fractions (*b*) and (*c*) both gave dicyclohexylurea, m. p. and mixed m. p. 232°; fraction (*d*) gave hexamethylenedi(cyclohexylurea), m. p. and mixed m. p. 230—232°.

Isopropylphenylcarbodi-imide. Phenyl isothiocyanate (54 g.) and isopropylamine (50 g.) were mixed in light petroleum (700 ml.). After an exothermic reaction had subsided, the mixture was heated under reflux for ½ hr. and then cooled. Colourless plates (73 g.) of isopropylphenylthiourea were collected and washed with light petroleum. The thiourea (73 g.) was added to a stirred suspension of yellow mercuric oxide (180 g.) in carbon disulphide (500 ml.). After the exothermic reaction had subsided, the mixture was heated for ½ hr., powdered calcium chloride (50 g.) and Hyflo Supercel (50 g.) were added, and the mixture was filtered and evaporated, giving the *carbodi-imide* (25 g.), b. p. 111—112°/14 mm. (Found: C, 74·5; H, 7·6; N, 17·8. $C_{10}H_{12}N_2$ requires C, 75·0; H, 7·6; N, 17·5%). Treatment with acetic acid gave isopropylphenylurea, m. p. 154—155° (lit.,[3] 156°) after recrystallisation from aqueous ethanol (Found: C, 67·7; H, 8·0; N, 15·5. Calc. for $C_{10}H_{14}N_2O$: C, 67·4; H, 7·9; N, 15·7%).

Disproportionation of isopropylphenylcarbodi-imide. The carbodi-imide (23·5 g.) was allowed to boil gently at atmospheric pressure under a 20″ Vigreux column. The liquid temperature rose steadily from 220° to 280° while the still-head temperature fell from 160° to 100°. The distillate (12·3 g.) was redistilled at 14 mm., to give di-isopropylcarbodi-imide (6·6 g.), b. p. 43—44°/14 mm. (Found: N, 22·0. Calc. for $C_7H_{14}N_2$: N, 22·2%), which with acetic acid gave di-isopropylurea, m. p. 190° (sublimes) (lit.,[4] 192°). The combined distillation residues were distilled at 14 mm. to give isopropylphenylcarbodi-imide (5·3 g.), b. p. 112—115°/14 mm., an intermediate fraction (2·0 g.), and diphenylcarbodi-imide (10·4 g.), b. p. 175—176°/14 mm. (Found: N, 14·4. Calc. for $C_{13}H_{10}N_2$: N, 14·4%), which with acetic acid gave diphenylurea, m. p. 237° (lit.,[5] 235°) (from acetone).

CIBA (A. R. L.) LIMITED,
DUXFORD, CAMBS.

[*Received, June 7th*, 1961.]

[3] Manguin, *Ann. Chim.* (*France*), 1911, **22**, 321.
[4] Hofmann, *Ber.*, 1882, **15**, 756.
[5] Weith, *Ber.*, 1876, **9**, 821.

998. *Phosphino-arylboranes.*

By G. E. Coates and J. G. Livingstone.

Phosphinodiarylboranes derived from monofunctional phosphines and boranes, *e.g.*, $Ph_2B{\cdot}PPh_2$ from Ph_2BCl and Ph_2PH, are monomeric and relatively resistant to hydrolysis and oxidation.[1] We now describe a few products derived from bifunctional phosphines or boranes.

Phenylphosphinidenebis(diphenylborane), $(Ph_2B)_2PPh$, from chlorodiphenylborane and phenylphosphine, and the analogous compound phenylbis(diphenylphosphino)borane, $(Ph_2P)_2BPh$, from dichlorophenylborane and diphenylphosphine, are both sensitive to atmospheric oxidation and are readily converted into the corresponding phenyl-substituted oxy-acids of boron and phosphorus by the action of aqueous alkaline hydrogen peroxide, *e.g.*:

$$(Ph_2P)_2BPh \longrightarrow 2Ph_2PO_2H + Ph{\cdot}B(OH)_2$$

Both these P–B compounds are colourless and are monomeric in benzene, but a yellow polymer is gradually deposited when a benzene solution of $(Ph_2P)_2BPh$ is heated under an inert atmosphere.

Dichlorophenylborane and phenylphosphine form a 1 : 1 complex, which slowly evolves hydrogen chloride when its solution in xylene is boiled. When hydrogen chloride evolution ceases, three products can be isolated: chloro(phenylphosphino)phenylborane, $PhClB{\cdot}PPhH$ (I), b. p. 98—100°/*ca.* 10^{-3} mm.; a colourless compound $(PhB{\cdot}PPh)_2$ (II), m. p. 89—91°, which is quantitatively oxidized to phenylboronic and phenylphosphonic acid; and a yellow involatile compound (III) containing just over 1% of chlorine. The most reasonable structure for compound (II) is cyclic. On the basis of our dipole-moment study of phosphinoboranes of the type $Ar_2B{\cdot}PAr'_2$, which indicated that phosphorus is a very weak π-donor to boron, we regard compound (II) as co-ordinatively unsaturated except for interaction with the phenyl groups.

(II)

The yellow product (III), which is insoluble in benzene, and yields phenylboronic and phenylphosphonic acids in the molar ratio 0·96 : 1 on oxidation, is probably a polymer containing B–Cl and P–H end groups: $PhBCl{-}[{-}PPh{\cdot}BPh{-}]_n{-}PPhH$. Its chlorine content indicates that n is about 13. A small P–H content was indicated by a weak infrared absorption at 4·33 μ. The amounts of products (I), (II), and (III) were in the approximate ratios 3 : 1 : 3.

Attempts to condense dichlorophenylborane and phenylphosphine in the presence of two mols. of triethylamine were not successful; only one mol. of amine hydrochloride separated but no crystalline product could be isolated from the two-phase benzene solution which probably contained the triethylammonium salt of a phosphinophenylborane anion.

In our earlier paper [1] on phosphinodiarylboranes, in which their dipole moments were shown to be in the direction $Ar_2\overrightarrow{B{\cdot}PAr_2}$, the polarity was ascribed mainly to electron flow from the aryl groups to the boron 2*p*-orbital, and similarly from the phosphorus atom to the aryl groups bound to it. As a check on this interpretation we hoped to measure the dipole moments of dimesityl- and di-(4-biphenylyl)-(di-*m*-tolylphosphino)borane. In the first compound we expected the steric requirements of the mesityl groups to prevent conjugation with the boron 2*p*-orbital, leading to a reduction of moment, while in the second compound the electron flow over a greater distance should result in a larger moment [than that of $Ph_2B{\cdot}P(C_6H_4Me\text{-}m)_2$]. The preparation of both compounds is described below, but they were too sparingly soluble to allow their dipole moments to be measured.

Experimental.—Preparations were carried out in a nitrogen atomosphere.

Phenylphosphinidenebis(diphenylborane), $(Ph_2B)_2PPh$. Chlorodiphenylborane (10 g., 0·05 mole) in dry xylene (50 c.c.) was slowly added to a mixture of triethylamine (6·5 c.c., 0·05 mole) and phenylphosphine (2·6 c.c., 0·025 mole) in xylene (50 c.c.). After the mixture had been

[1] Coates and Livingstone, *J.*, 1961, 1000.

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refluxed for 24 hr., cooled, and filtered from triethylammonium chloride, evaporation yielded the *phosphine*, which was crystallized from benzene–hexane and had m. p. 148—150° (Found: C, 81·8; H, 5·6. Found, by hydrogen peroxide oxidation: PhP, 24·2; Ph_2B, 75·1. $C_{30}H_{25}B_2P$ requires C, 82·2; H, 5·7; PhP, 24·7; Ph_2B, 75·3%). The degree of association, measured cryoscopically at 0·125, 0·151, 0·249, and 0·317 weight % in benzene solution, was 0·99, 1·01, 1·04, and 1·19.

Bis(diphenylphosphino)phenylborane, $PhB(PPh_2)_2$. Dichlorophenylborane, m. p. 5·1—5·5° (4·0 g., 0·025 mole), in benzene (30 c.c.) was added to a solution of diphenylphosphine (9·3 g., 0·05 mole) and triethylamine (5·1 g., 0·05 mole) in benzene (50 c.c.) at room temperature. The mixture was refluxed for 24 hr., cooled, and filtered under nitrogen from triethylammonium chloride. The filtrate was evaporated and the yellow residue extracted with benzene, leaving a small amount of yellow insoluble polymer. The colourless *product* (9·2 g., 78%) crystallized from benzene–hexane and had m. p. 143—144° (Found, by oxidation: PhB, 17·5; Ph_2P, 79·8. $C_{30}H_{25}BP_2$ requires PhB, 18·0; Ph_2P, 80·9%). The degree of association, measured cryoscopically at 0·733, 1·101 and 1·124 weight % in benzene solution, was 0·92, 1·01, and 1·03.

Prolonged heating of the colourless monomer in benzene yielded more of the insoluble yellow polymer, m. p. 120—132° (Found, by oxidation: PhB, 16·0; Ph_2P, 79·9%). No halogen could be detected in the yellow product, which was insoluble in all common organic solvents. Both monomer and polymer were unaffected by boiling dilute aqueous acid or alkali.

Reaction between phenylphosphine and dichlorophenylborane. Dichlorophenylborane (4·0 g., 0·025 mole) in dry hexane (20 c.c.) was slowly added to an equimolar amount of phenylphosphine (2·8 g.) in the same solvent (20 c.c.) contained in a double Schlenk tube equipped with a sintered filter disc.[2] The colourless crystalline and extremely hygroscopic *adduct* was collected by filtration under nitrogen, washed with solvent, and dried by pumping [6·4 g., 75%; m. p. 62—64° (sealed tube)] (Found: Cl, 26·5, 26·8. $C_{12}H_{12}BCl_2P$ requires Cl, 26·4%).

A mixture of phenylphosphine (11·0 g., 0·1 mole) and dichlorophenylborane (15·9 g., 0·1 mole) in xylene was refluxed until evolution of hydrogen chloride had apparently ceased (16 hr.). The solvent was evaporated, and then vacuum distillation yielded *chlorophenyl(phenylphosphino)borane* [PhPH·BClPh] (I) (10·5 g.), b. p. 98—100°/*ca.* 10^{-3} mm., as a colourless fuming liquid (Found: Cl, 15·7, 16·1; PhB, by hydrolysis, 38·2. $C_{12}H_{11}BClP$ requires Cl, 15·4; PhB, 38·1%).

The orange glassy residue from the distillation was extracted with hot benzene. Evaporation of the extract yielded the colourless *tetraphenyl-1,3-diphospha-2,4-diboretan* (II) (3·6 g.), m. p. 89—91° (Found, by oxidation: PhB, 44·7; PhP, 55·6. $C_{24}H_{20}B_2P_2$ requires PhB, 44·8; PhP, 55·2%). The molecular weight, cryoscopically at 0·515, 0·874, 1·164, and 1·593 weight % in benzene, was 340, 344, 356, and 375 ($C_{24}H_{20}B_2P_2$ requires *M*, 344). The orange-yellow residue (III) from the benzene extraction (11·5 g.) had m. p. 168—175° (Found: Cl, 1·3; by oxidation, PhB, 42·8; PhP, 50·5%).

*Dimesityl(di-*m*-tolylphosphino)borane.* The sodium derivative of di-*m*-tolylphosphine (0·025 mole) in tetrahydrofuran (50 c.c.) was slowly added to fluorodimesitylborane[3] (6·7 g., 0·025 mole) in the same volume of solvent at −30°. The mixture was then allowed to come to room temperature, boiled for 1 hr. under reflux, and filtered. Evaporation of the filtrate yielded 1·2 g. of *product*, but the main bulk was an insoluble residue left when sodium fluoride had been dissolved out of the white precipitate by washing it with water. The total amount of product recovered was 5·4 g. (47%), and the m. p. 264—265° (Found: C, 81·5; H, 8·2. Found, by oxidation: $mesityl_2B$, 55·3; *m*-$tolyl_2P$, 45·2. $C_{32}H_{36}BP$ requires C, 82·6; H, 7·9; $mesityl_2B$, 55·3; *m*-$tolyl_2P$, 45·7%).

We were unable to prepare this compound from fluorodimesitylborane, di-*m*-tolylphosphine, and triethylamine in boiling benzene or xylene.

*Di-(4-biphenylyl)(di-*m*-tolylphosphino)borane*, $[(m\text{-}CH_3\cdot C_6H_4)_2P\cdot B(p\text{-}C_6H_5\cdot C_6H_4)_2]$, m. p. 77—78°, was obtained in 46% yield from the phosphine, chlorodi-4-biphenylylborane, and triethylamine in boiling benzene [Found: C, 85·8; H, 5·9. Found, by oxidation: $(p\text{-}C_6H_5\cdot C_6H_4)_2B$, 58·6; *m*-$tolyl_2P$, 39·9. $C_{38}H_{32}BP$ requires C, 86·0; H, 6·0; $(p\text{-}C_6H_5\cdot C_6H_4)_2B$, 59·9; *m*-$tolyl_2P$, 40·1%]. Both this and the preceding compound were insoluble in ether, hydrocarbons, acetone, ethyl methyl ketone, chloroform, and carbon tetrachloride.

Infrared spectra.—The mesityl and the 4-biphenylyl compound had very strong absorption

[2] Fischer, Hafner, and Stahl, *Z. anorg. Chem.*, 1955, **282**, 47.
[3] Brown and Dodson, *J. Amer. Chem. Soc.*, 1957, **79**, 2305.

bands at 1435 and 1497 cm.$^{-1}$, respectively (pressed in potassium iodide discs), which we assign to a B–P stretching vibration. Both bands showed the isotopic splitting commonly found in the spectra of boron compounds. It is significant that the B–P frequency of the mesityl compound is less than that of any other diarylphosphinodiarylborane we have studied, and that of the 4-biphenylyl compound is greater.

The infrared spectra of the other phosphinoarylboranes described in this Note were generally too complex for assignments to be made.

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999. *Thiophthalimides.*

By R. J. W. CREMLYN.

THE only members of this group of compounds recorded in the literature are mono- and di-thiophthalimide,[1] *N*-phenylthiophthalimide,[2] and *N*-butylthiophthalimide.[3]

The *N*-substituted monothiophthalimides described in this paper were prepared from the corresponding *N*-aryl-[4] or *N*-alkyl-phthalimide [5] by reaction with phosphorus pentasulphide (1 mole) in boiling xylene for 5—6 hours. For the dithiophthalimides 2 moles of phosphorus pentasulphide were used and heating was continued for 8—12 hours. The purification of the products was often difficult, especially that of the lower *N*-alkyl derivatives, which were usually low in sulphur content. There was sometimes extensive decomposition and "mixed crystal" formation between the corresponding mono- and di-thiophthalimides.

The thiophthalimides are, apparently, more stable than thiosuccinimides, because they could not be converted into the corresponding thiophthalamic acids by treatment with aqueous ethanolic sodium hydroxide (cf. ref. 6). The thiophthalimides were synthesised as potential fungicides, and to assist in their identification in plant tissue their ultraviolet absorption spectra were determined. The *N*-alkylthiophthalimides (in ethanol) exhibit three characteristic maxima, at 220—225, 295—300, and 330—335 mμ (ε 22,000—24,000, 8000—9000, and 7000—8000, respectively). The same three absorption bands are also shown by the *N*-arylthiophthalimides, except that these have shifted slightly (~5 mμ) in the direction of longer wavelength. The maximum at 295—300 mμ is absent from dithiophthalimides, but the two other characteristic bands are again present, though they have moved 5—10 mμ in the direction of longer wavelength. Also the intensity of the band at 340—360 mμ has approximately doubled; this peak is due to the presence of the thiocarbonyl group, which is known to give an absorption maximum at ~330 mμ.[7] The additional band at 235—245 mμ is also probably due to this group,[8] as phthalimides exhibited bands at 221 and 290 mμ only. These last maxima are almost certainly functions of the absorption of the carbonyl group in conjugation with the benzene nucleus (cf. succinimides, which do not show peaks in this region [9]).

Experimental.—*N-Substituted phthalimides.* The arylphthalimides were generally prepared by boiling phthalic anhydride and the appropriate arylamine in glacial acetic acid, as described by Vanags.[4] The higher *N*-alkylphthalimides were best obtained by heating a mixture of

[1] Drew and Kelly, *J.*, 1941, 627, 630.
[2] Reissert and Holle, *Ber.*, 1911, **44**, 3033.
[3] Baguley and Elvidge, *J.*, 1957, 709.
[4] Vanags, *Acta Univ. Latviensis, Kim. Fakultat*, 1939, Ser. 4, No. 8, 405; *Ber.*, 1942, **75**, 719.
[5] Rice, Reid, and Grogan, *J. Org. Chem.*, 1954, **19**, 884.
[6] Reissert and Moré, *Ber.*, 1906, **39**, 3298.
[7] Braude, *Ann. Reports*, 1945, **42**, 112.
[8] Gillam and Stern, "An Introduction to Electronic Absorption Spectra," Arnold, London, 1954, p. 49.
[9] Turner, *J.*, 1957, 4555.

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phthalic anhydride and the alkylamine at 160—170°, following the procedure used for the preparation of *N*-alkylsuccinimides.[5] The lower members were obtained by heating a mixture of phthalimide, anhydrous potassium carbonate, and the appropriate alkyl halide in anhydrous dimethylformamide.[10]

Thiophthalimides. The general preparative procedure was as follows: The *N*-substituted phthalimide (10—20 g.) was dissolved in xylene (200—400 c.c.) and heated at ~100°. Then finely divided phosphorus pentasulphide (1 mole) was added with mechanical stirring, and the mixture gently boiled under reflux. After 1 hr. the liquid generally darkened, and heating was continued until slight further darkening occurred (4—5 hr.). The mixture was filtered hot, allowed to cool, and refiltered. The xylene was removed under reduced pressure, and the dark brown oil dissolved in hot ethanol (charcoal), filtered through " Hyflo-supercel," and evaporated under reduced pressure to the point of crystallisation, the crude solid being purified by recrystallisation from this solvent. If the product was a liquid, it was purified by high-vacuum distillation. For the preparation of dithiophthalimides the general procedure was similar, except that 2 moles of phosphorus pentasulphide were used, and the heating period was increased to 8—12 hr.

Attempted preparation of N-methoxyphenylthiophthalamic acid. *N*-(*o*-Methoxyphenyl)-thiophthalimide (4 g.) was treated with 10% sodium hydroxide solution (35 c.c., 5 moles) and

N-Alkylthiophthalimides.

N-Subst.	M. p./b. p.	Yield (%)	Formula	Found (%) C	H	N	S	Reqd. (%) C	H	N	S
Me	94—96°	34	C_9H_7NOS	61·9	3·9	8·0	18·7	62·3	3·9	7·9	18·2
Cl·CH_2	85—88	60	C_9H_6ClNOS	46·6	2·9	6·8	15·6	46·3	2·8	6·6	15·2
EtO_2C·CH_2	46—50	48	$C_{13}H_{11}NO_2S$	57·4	4·4	5·7	12·0	57·8	4·4	5·6	12·2
n-C_6H_{13}	125—130/0·1 mm.	54	$C_{14}H_{17}NOS$	68·4	6·7	5·9	12·2	68·0	6·9	5·7	12·8
n-C_8H_{17}	150—154/0·3	65	$C_{16}H_{21}NOS$	69·6	7·4	5·1	10·9	69·8	7·6	5·1	11·5
n-C_9H_{19}	180—185/0·2	63	$C_{17}H_{23}NOS$	70·7	7·7	4·5	10·8	70·6	7·9	4·8	11·0
n-$C_{16}H_{33}$	54—56	72	$C_{24}H_{37}NOS$	75·0	9·3	3·6	7·9	74·4	9·6	3·6	8·3

N-Arylthiophthalimides.

4-Cl·C_6H_4	158—160°	40	$C_{14}H_8ClNOS$	61·8	3·1	4·9	12·0	61·5	2·9	5·1	11·7
2-Cl·C_6H_4	108—110	48	$C_{14}H_8ClNOS$	62·0	2·8	5·1	11·8	61·5	2·9	5·1	11·7
3-Cl·C_6H_4	144—146	30	$C_{14}H_8ClNOS$	61·3	2·9	4·8	11·2	61·5	2·9	5·1	11·7
4-MeO·C_6H_4	134—136	41	$C_{15}H_{11}NO_2S$	67·3	4·1	5·1	11·5	66·9	4·1	5·2	11·9
2-MeO·C_6H_4	108—110	65	$C_{15}H_{11}NO_2S$	67·0	4·3	5·0	12·0	66·9	4·1	5·2	11·9
3-Me·C_6H_4	156—160	28	$C_{15}H_{11}NOS$	72·1	4·3	5·5	12·2	72·5	4·4	5·9	12·1
2,4-$Me_2C_6H_3$	126—128	58	$C_{16}H_{13}NOS$	72·2	4·8	5·2	11·5	71·9	4·9	5·2	12·0
2,5-$Me_2C_6H_3$	104—106	70	$C_{16}H_{13}NOS$	72·4	4·9	5·0	11·6	71·9	4·9	5·2	12·0

Dithiophthalimides.

Ph	150—153	22	$C_{14}H_9NS_2$	65·4	4·0	6·0	25·2	65·9	3·5	5·5	25·1
2-Me·C_6H_4	128—130	50	$C_{15}H_{11}NS_2$	67·2	3·9	5·2	23·4	66·9	4·1	5·2	23·8
4-Me·C_6H_4	148—150	17	$C_{15}H_{11}NS_2$	67·3	4·1	4·9	23·5	66·9	4·1	5·2	23·8
4-MeO·C_6H_4	122—124	10	$C_{15}H_{11}NOS_2$	63·1	3·6	5·0	21·9	63·2	3·7	4·9	22·5
α-$C_{10}H_7$	148—149	37	$C_{18}H_{11}NS_2$	71·0	3·6	4·6	21·7	70·8	3·6	4·6	22·0
Cl·CH_2	115—117	20	$C_9H_6ClNS_2$	47·2	2·7	6·0	28·2	47·4	2·6	6·1	28·1

the suspension warmed (together with 5 c.c. of ethanol) for 3 hr. at 80—90°. Most of the solid dissolved; the mixture was filtered, acidified with dilute hydrochloric acid, and extracted with ether (250 c.c.). The extract was washed three times with water, dried (Na_2SO_4), filtered, and evaporated. The residue was unchanged *o*-methoxyphenylthiophthalimide, m. p. and mixed m. p. 108—110°. Similar unsuccessful attempts were made to hydrolyse nine other thiophthalimides, and in each case the starting material was recovered unchanged.

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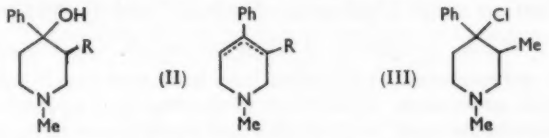
[10] Billman and Cash, *Proc. Indiana Acad. Sci.*, 1952, **62**, 158.

1000. *Action of Thionyl Chloride upon Alcohols derived from Alpha- and Beta-prodine.**

By A. F. Casy.

Evidence for the configurations of epimeric alicyclic alcohols can be obtained from results of their reactions with thionyl chloride. Thus Maurit and Preobrazhenskii [1] assigned *cis*- and *trans*-configurations to isomers of methyl 4-hydroxy-1-methylpiperidine-3-carboxylate that gave arecoline and the chloro-compound, respectively, after such treatment.

Reaction between 1,3-dimethyl-4-phenylpiperidin-4-ol (I; R = Me), derived from alphaprodine by alkaline hydrolysis, and thionyl chloride gave a mixture in which the tetrahydropyridine (II; R = Me) hydrochloride predominated.



Evidence that the minor components were the chloro-compound (III) and the alcohol (I; R = Me) hydrochlorides is provided by the results of chlorine analysis and by infrared absorption studies. The mixture could not be satisfactorily separated by crystallization. The chloro-compound was unstable since solution of the mixture in water, liberation of basic material with ammonia, and reconversion of base into salt, gave the pure tetrahydropyridine (II; R = Me) hydrochloride. McElvain and Safranski [2] obtained similar results with 1-methyl-4-phenylpiperidin-4-ol (I; R = H). In contrast, reaction between thionyl chloride and the epimeric alcohol (from betaprodine) gave a high yield of the chloro-compound (III) hydrochloride that could be recovered after treatment with aqueous ammonia.

Evidence for the same conformation of the hydroxyl group in 1,3-dimethyl-4-phenylpiperidin-4-ol from alphaprodine and in 1-methyl-4-phenylpiperidin-4-ol is provided by their identical reactions with thionyl chloride, axially-placed hydroxy-groups, expected in the more stable (chair) conformation of the alcohol (I; R = H), and chloro-groups providing the required stereochemical conditions for ionic eliminations. Isolation of a stable chloro-compound from the alcohol from betaprodine shows the last to differ from the above alcohols in respect of hydroxyl conformation which is, therefore, equatorial in the alcohol from betaprodine. This interpretation is consistent with assigned configurations [3] (3-Me, 4-Ph *trans* and *cis* for alpha- and beta-prodine, respectively).

Experimental.—A stirred solution of 1,3-dimethyl-4-phenylpiperidin-4-ol (5·0 g.), m. p. 100—101°, derived from alphaprodine,[4] in dry chloroform (25 ml.) was cooled to −20° and treated with freshly distilled thionyl chloride (6·5 g.) in dry chloroform (25 ml.), added dropwise. The addition was complete after 20 min., and the mixture was then heated under reflux for 4 hr., cooled, and diluted with ether. Crystals separated on storage at 5°. Recrystallization from ethanol–ether gave material, m. p. 191—192°, depressed to 189° on mixing with pure tetrahydro-1,3-dimethyl-4-phenylpyridinium chloride, m. p. 187°;[5] it had $\lambda_{max.}$ 236 mμ (ε 9650) in water and a small absorption peak at 3450 cm.$^{-1}$ [cf. pure pyridine derivative, $\lambda_{max.}$ 236 mμ (ε 11,230)] (Found: Cl, 16·85%; equiv., 231. Calc. for $C_{13}H_{18}NCl$: Cl, 15·9%; equiv., 224). The mixture in water was made alkaline with aqueous ammonia and the base extracted with ether. After being dried (Na_2SO_4), the solvent was removed; the residue, after treatment with ethanolic hydrogen chloride, gave tetrahydro-1,3-dimethyl-4-phenylpyridinium chloride, m. p. and mixed m. p. 187—188°.

* These are General Medical Council's approved names for α- and β-1,3-dimethyl-4-phenyl-4-propionyloxypiperidine.

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[2] McElvain and Safranski, *J. Amer. Chem. Soc.*, 1950, **72**, 3134.
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Treatment of 1,3-dimethyl-4-phenylpiperidin-4-ol (2·0 g.), m. p. 118°, derived from betaprodine,[4] with thionyl chloride (2·9 g.) as above gave *4-chloro-1,3-dimethyl-4-phenylpiperidinium chloride* (1·4 g.), m. p. 154° after recrystallization from ethanol–ether (Found: C, 59·9; H, 7·3; N, 5·45; Cl, 27·05%; equiv., 263. Calc. for $C_{13}H_{19}Cl_2N$: C, 60·0; H, 7·3; N, 5·4; Cl, 27·3%; equiv., 260). This hydrochloride was recovered after treatment with aqueous ammonia as above.

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1001. 1,2-*Dihydro*-1,4-*dihydroxy*-2-*oxoquinolines Preparation by Reductive Cyclisation with Hydrazine Hydrate and Palladium–Charcoal.*

By R. T. Coutts, M. Hooper, and D. G. Wibberley.

Hydroxamic acids related to quinoline have been prepared by oxidation of 2-ethoxyquinolines with subsequent hydrolysis,[1] cyclisation of *o*-hydroxyaminophenylpropiolic acid with hydrochloric acid,[2] or reductive cyclisation of a suitable *o*-nitro-acid or -ester.[3] These methods either involve the use of relatively inaccessible starting materials or yield the hydroxamic acid as the minor product of reaction. Dewar and Mole [4] have shown that certain aromatic nitro-compounds are readily reduced to the corresponding amines by the action of hydrazine hydrate in the presence of palladium–charcoal. We have shown that the reduction of methyl or ethyl *o*-nitrobenzoylacetate under these conditions gives a very good yield of 1,2-dihydro-1,4-dihydroxy-2-oxoquinoline. Attempts to extend the method to the synthesis of a series of 3-substituted analogues were only partly successful. In the attempted reductive cyclisation of methyl α-bromo-α-*o*-nitrobenzoylacetate concurrent reduction of the bromo-group took place, and in the reduction of methyl or ethyl *o*-nitrobenzoylacetoacetate the acetyl group was removed by hydrolysis. Both reactions yielded 1,2-dihydro-1,4-dihydroxy-2-oxoquinoline as sole product. Side reactions also preponderated in the attempted reductive cyclisation of ethyl α-cyano-α-*o*-nitrobenzoylacetate where the products were anthranilic acid and a compound presumed to be 4-amino-1,2,4-triazole-3,5-diacethydrazide, and in the case of diethyl *o*-nitrobenzoylmalonate where the only identifiable product was malonhydrazide. Reductive cyclisation of methyl or ethyl α-*o*-nitrobenzoylpropionate by the same method gave an excellent yield of 1,2-dihydro-1,4-dihydroxy-3-methyl-2-oxoquinoline and, in an analogous manner, methyl α-(*o*-nitrobenzoyl)butyrate yielded the 3-ethylquinolone.

Dewar and Mole [4] found that reduction to the amino-group occurred almost instantaneously with very reactive nitro-derivatives of hydrocarbons, and with *p*-nitroanisole, but that nitrobenzene itself was reduced only slowly. The very good yields of hydroxamic acids obtained in this preliminary study, however, suggest that at least the partial reduction of the nitro-group is enhanced by an electron-attracting substituent in the *ortho*-position.

Experimental.—Methyl o-nitrobenzoylacetoacetate. The sodium derivative of methyl acetoacetate (122 g.) was treated with a solution of *o*-nitrobenzoyl chloride (185 g.) in benzene as described by Gabriel and Gerhard [5] for the ethyl ester. The *acetoacetate* (128 g.) separated from ethanol in prisms, m. p. 91—92° (Found: C, 53·8; H, 4·2; N, 5·2. $C_{12}H_{11}NO_6$ requires C, 54·3; H, 4·2; N, 5·3%).

Methyl o-nitrobenzoylacetate. The potassium derivative of the above acetoacetate (32 g.) in water (100 ml.) was stirred at 80—90° for 10 min. with ammonium chloride (10 g.). The oil which separated was removed. The operations were repeated a further 3 times with fresh additions of ammonium chloride. The combined red oil was converted into the potassium

[1] Newbold and Spring, *J.*, 1948, 1864; Cunningham, Newbold, Spring, and Stark, *J.*, 1949, 2091.
[2] Arndt, Ergener, and Kutlu, *Chem. Ber.*, 1953, **86**, 957.
[3] Friedlander and Ostermaier, *Ber.*, 1881, **14**, 1916; 1882, **15**, 332; Friedlander, *Ber.*, 1914, **47**, 3369; Heller and Wunderlich, *Ber.*, 1914, **47**, 2889.
[4] Dewar and Mole, *J.*, 1956, 2556.
[5] Gabriel and Gerhard, *Ber.*, 1921, **54**, 1069.

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derivative (22 g.) by treatment with potassium hydroxide in ethanol, and the *acetate* (15·2 g.) liberated from a solution of this derivative in water by the passage of carbon dioxide. Crystallisation from ether–light petroleum gave prisms, m. p. 41—42° (Found: C, 54·0; H, 4·05; N, 6·3. $C_{10}H_9NO_5$ requires C, 53·8; H, 4·07; N, 6·3%).

Methyl α-bromo-α-o-nitrobenzoylacetate. Bromination of methyl *o*-nitrobenzoylacetate (1·5 g.) in carbon tetrachloride at room temp. gave the *bromo-acetate* (1·6 g.), crystallising from ethanol in pale yellow needles, m. p. 83—84° (Found: N, 4·6. $C_{10}H_8BrNO_5$ requires N, 4·6%).

Methyl α-o-nitrobenzoylbutyrate. The potassium derivative of methyl *o*-nitrobenzoylacetate (3·4 g.), ethyl iodide (3·0 ml.), and acetone (25 ml.) were refluxed for 5 hr. The mixture was diluted with water and the liberated oil extracted into ether and distilled, to yield a pale yellow *product* (2·1 g.), b. p. 140—142°/3·0 mm. (Found: C, 57·8; H, 5·9; N, 5·9. $C_{12}H_{13}NO_5$ requires C, 57·4; H, 5·2; N, 5·6%).

Methyl α-o-nitrobenzoylpropionate. This compound was obtained as an orange oil in the same manner from methyl iodide and methyl *o*-nitrobenzoylacetate but was not distilled before further reaction (Found: N, 5·8. Calc. for $C_{11}H_{11}NO_5$: N, 5·9%).

1,2-*Dihydro*-1,4-*dihydroxy*-2-*oxoquinoline.* (*a*) Methyl *o*-nitrobenzoylacetate (1·0 g.), 10% palladium–charcoal (0·1 g.), hydrazine hydrate (1·0 ml.), and ethanol (12 ml.) were refluxed for 30 min., a further 1·0 ml. of hydrazine hydrate was then added and refluxing continued for a further 30 min. The mixture was cooled, and the product and catalyst were collected and suspended in 2·0% sodium hydroxide (20 ml.). The suspension was filtered and the filtrate acidified with hydrochloric acid, to yield the quinolone (0·56 g.), m. p. 275—276° (decomp.), not raised on crystallisation from acetic acid (Found: C, 60·7; H, 3·8; N, 7·7. Calc. for $C_9H_7NO_3$: C, 61·0; H, 4·0; N, 7·9%). A similar reaction with more hydrazine hydrate (5·0 ml.) but reduced time (5 min.) gave a lower yield (0·48 g.) of the same quinolone. The quinolone was soluble in sodium hydrogen carbonate solution with evolution of carbon dioxide and gave a blue-green colour with ferric chloride. The dimethyl ether melted at 119—120° (Found: N, 6·8. Calc. for $C_{11}H_{11}NO_3$: N, 6·8%). Arndt *et al.*[2] give m. p. 276° (decomp.) for the quinolone and 124° for the dimethyl ether. The following compounds gave, in the yields stated, the same quinolone, identified in each case by its reactions with sodium hydrogen carbonate and ferric chloride, and its m. p. and mixed m. p.: ethyl *o*-nitrobenzoylacetate (88%), methyl (48%) and ethyl *o*-nitrobenzoylacetoacetate (51%), and methyl α-bromo-α-*o*-nitrobenzoylacetate (18%).

1,2-*Dihydro*-1,4-*dihydroxy*-3-*methyl*-2-*oxoquinoline.* Ethyl α-*o*-nitrobenzoylpropionate [5] (2·2 g.) was treated with hydrazine hydrate and palladium–charcoal under the above conditions. The mixture was filtered and evaporated to dryness. Trituration with dilute hydrochloric acid yielded the 3-*methylquinolone* (1·63 g.) which separated from acetic acid in prisms, m. p. 254—256° (decomp.) (Found: C, 63·0; H, 5·0; N, 7·1. $C_{10}H_9NO_3$ requires C, 62·9; H, 4·75; N, 7·3%). Reductive cyclisation of methyl α-*o*-nitrobenzoylpropionate gave the same product which was soluble in sodium hydrogen carbonate and gave a blue colour with ferric chloride.

3-*Ethyl*-1,2-*dihydro*-1,4-*dihydroxy*-2-*oxoquinoline.* In the manner described above for the 3-methylquinolone, methyl α-*o*-nitrobenzoylbutyrate (1·1 g.) was converted into this 3-*ethylquinolone* (0·87 g.) which separated from acetic acid in prisms, m. p. 223—224° (decomp.) (Found: C, 63·8; H, 5·4; N, 7·0. $C_{11}H_{11}NO_3$ requires C, 64·4; H, 5·4; N, 6·8%). The product was soluble in sodium hydrogen carbonate and gave a blue colour with ferric chloride.

Attempted reductive cyclisation of ethyl α-cyano-α-o-nitrobenzoylacetate. From an attempted reductive cyclisation of ethyl α-cyano-α-*o*-nitrobenzoylacetate (1·0 g.) the filtrate deposited a solid (0·14 g.), m. p. 182° (from ethanol). This product was presumed to be 4-amino-1,2,4-triazole-3,5-diacethydrazide (Found: C, 31·3; H, 5·7; N, 49·9. Calc. for $C_6H_{12}N_8O_2$: C, 31·6; H, 5·3; N, 49·2%), since nitriles are known to form similar 4-aminotriazoles on treatment with aqueous hydrazine.[6] The filtrate from the product was evaporated to dryness and the residual solid triturated with dilute hydrochloric acid, to yield anthranilic acid (0·28 g.), m. p. and mixed m. p. 144—145°.

Attempted reductive cyclisation of diethyl o-nitrobenzoylmalonate. From an attempted reductive cyclisation of diethyl *o*-nitrobenzoylmalonate (1·9 g.) the filtrate deposited plates of malonhydrazide (0·32 g.), m. p. 153—154° (Found: N, 42·4. Calc. for $C_3H_6N_4O_2$: N, 42·4%).

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[6] Migrdichian, "The Chemistry of Organic Cyanogen Compounds," Reinhold Publ. Corp., New York, 1947, p. 74.

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1002. *π-Molecular Complex of Hexamethylborazole with Tetracyanoethylene.*

By N. G. S. Champion, R. Foster, and R. K. Mackie.

The aromatic structure of borazole and substituted borazoles suggests that these molecules might form π-bonded intermolecular charge-transfer complexes [1] with other suitable molecules. In particular, the stability of such a complex of an electron acceptor with hexamethylborazole should be favoured because of the expected low ionisation potential of hexamethylborazole relative to borazole. Charge-transfer complexes usually have a broad featureless absorption band. In solution these complexes are in equilibrium with the component molecules, and cooled solutions, in which complex formation is increased, consequently show an intensification of this absorption.

Mixtures of hexamethylborazole (*b*) and tetracyanoethylene (*a*) in chloroform solution have such a band, not possessed by either component alone. The intensity of the band slowly decreases with time at room temperature which suggests that there is further reaction. From measurements of optical density of solutions of mixtures of the two components at various concentrations soon after mixing, the absorption may be attributed to a very weak complex (*c*) with a ratio of $a : b$ of 1 : 1, for which, at 21°, the association constant $K = 0{\cdot}7 \pm 0{\cdot}3$ l. mole^{-1} (where $K = [c]/[a][b]$, all concentrations in mole l.$^{-1}$): $\varepsilon_{max.} = 2000 \pm 500$, $\lambda_{max.} = 461$ mμ. The corresponding values for the hexamethylbenzene–tetracyanoethylene complex in chloroform at 21° are:

$$K = 27{\cdot}6 \pm 0{\cdot}5 \text{ l. mole}^{-1};\ \varepsilon_{max.} = 5080 \pm 90;\ \lambda_{max.} = 540 \text{ mμ}.$$

McConnell, Ham, and Platt [2] demonstrated the empirical relation between the ionisation potentials (I_p) of the donor molecules and the frequencies of the charge-transfer bands of complexes of the respective donor molecules with a given acceptor. Although there is no theoretical basis for this observation,[3] it appears to hold for a wide variety of molecular complexes.[4] Comparison of the frequency of the charge-transfer band of the hexamethylborazole–tetracyanoethylene complex with the frequencies of complexes of other donor molecules of known ionisation potential with tetracyanoethylene suggests that hexamethylborazole has $I_p \approx 8{\cdot}5$ ev, if this linear relationship is valid. Solutions of hexamethylborazole with chloranil in chloroform also show absorption additional to that of the components. This appears as a band ($\lambda_{max.} = 380$ mμ) which is close to a transition of chloranil but intensifies on cooling. By an application of the above empirical relation, the transition of the chloranil complex would correspond to $I_p \approx 8{\cdot}7$ ev for hexamethylborazole.

Experimental.—Materials. Hexamethylborazole was prepared *via* *NN'N''*-trimethylborazole [5] by Smalley and Stafiej's method,[6] and recrystallised from acetonitrile; it had m. p. 99° (Wiberg and Hertwig [7] give 99°). Tetracyanoethylene was prepared by the method of Cairns and his co-workers,[8] recrystallised from chlorobenzene, and thrice sublimed, having m. p. 198°. Chloroform and hexamethylbenzene were purified as described in an earlier paper.[9]

Analytical. Solutions were made up gravimetrically, and their optical densities were measured with an Optical CF4 spectrophotometer and a silica 10 mm. cuvette in a thermostatically controlled water-jacketed holder. The equilibrium constant for the hexamethylborazole complex was evaluated by Rose and Drago's method,[10] and for the hexamethylbenzene complex by Foster, Hammick, and Wardley's method.[11]

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[9] Foster, *J.*, 1960, 1075. [10] Rose and Drago, *J. Amer. Chem. Soc.*, 1959, **81**, 6138.
[11] Foster, Hammick, and Wardley, *J.*, 1953, 3817.

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